536/024.100; 935/006.000; 935/034.000; 935/059.000;
935/062.000
NCL NCLM: 514/044.000
NCLS: 424/001.110; 424/001.490; 424/001.610; 424/001.650;
424/001.690; 424/093.200; 424/093.210; 424/450.000;
435/069.100; 435/069.500; 435/320.100; 536/024.100

(FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, LIFESCI, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, USPATFULL' ENTERED AT 10:30:16 ON 09 MAY 2000)

L37 546 S BEHR T?/AU
L38 3233 S GOLDENBERG D?/AU
L39 240 S L37 AND L38
L40 245 S (L39 OR L37 OR L38) AND (RENAL? OR KIDNEY)
L41 31 S L40 AND (L3 OR (D OR L)(W)(LYSINE OR LYS))
L42 11 DUP REM L41 (20 DUPLICATES REMOVED)

L42 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 1
ACCESSION NUMBER: 1999:368541 CAPLUS
DOCUMENT NUMBER: 131:155360
TITLE: Higher-linear energy transfer (LET) .alpha. versus low-LET .beta. emitters in radioimmunotherapy of solid tumors: therapeutic efficacy and dose-limiting toxicity of 213Bi- versus 90Y-labeled CO17-1A fab' fragments in a human colonic cancer model
AUTHOR(S): **Behr, Thomas M.**; Behe, Martin; Stabin, Michael G.; Wehrmann, Eike; Apostolidis, Christos; Molinet, Roger; Strutz, Frank; Fayyazi, Afshin; Wieland, Eberhard; Gratz, Stefan; Koch, Lothar; **Goldenberg, David M.**; Becker, Wolfgang
CORPORATE SOURCE: Departments of Nuclear Medicine, Georg-August-University, Gottingen, D-37075, Germany
SOURCE: Cancer Res. (1999), 59(11), 2635-2643
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: AACR Subscription Office
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Recent studies suggest that radioimmunotherapy (RIT) with high-linear energy transfer (LET) radiation may have therapeutic advantages over conventional low-LET (e.g., .beta.-) emissions. Furthermore, fragments may be more effective in controlling tumor growth than complete IgG. However, to the best of our knowledge, no investigators have attempted a direct comparison of the therapeutic efficacy and toxicity of a systemic targeted therapeutic strategy, using high-LET .alpha. vs. low-LET .beta. emitters in vivo. The aim of this study was, therefore, to assess the toxicity and antitumor

efficacy of RIT with the .alpha. emitter 213Bi/213Po, as compared to the .beta. emitter 90Y, linked to a monovalent Fab' fragment in a human colonic cancer xenograft model in nude mice. Biodistribution studies of 213Bi- or 88Y-labeled benzyl-diethylene-triamine-pentaacetate-conjugated Fab' fragments of the murine monoclonal antibody CO17-1A were performed in nude mice bearing s.c. human colon cancer xenografts. 213Bi was readily obtained from an "inhouse" 225Ac/213Bi generator. It decays by .beta.- and 440-keV .gamma. emission, with a t1/2 of 45.6 min, as compared to the ultra-short-lived .alpha. emitter, 213Po (t1/2 = 4.2 .mu.s). For therapy, the mice were injected either with 213Bi- or 90Y-labeled CO17-1A Fab', whereas control groups were left untreated or were given a radiolabeled irrelevant control antibody. The max. tolerated dose (MTD) of each agent was detd. The mice were treated with or without inhibition of the **renal** accretion of antibody fragments by **D-lysine**, bone marrow transplantation, or combinations thereof. Myelotoxicity and potential second-organ toxicities, as well as tumor growth, were monitored at weekly intervals. Addnl., the therapeutic efficacy of both 213Bi- and 90Y-labeled CO17-1A Fab' was compared in a GW-39 model metastatic to the liver of nude mice. In accordance with **kidney** uptake values of as high as .gtoreq.80% of the injected dose per g, the **kidney** was the first dose-limiting organ using both 90Y- and 213Bi-labeled Fab' fragments. Application of **D-lysine** decreased the **renal** dose by >3-fold. Accordingly, myelotoxicity became dose limiting with both conjugates. By using lysine protection, the MTD of 90Y-Fab' was 250 .mu.Ci and the MTD of 213Bi-Fab' was 700 .mu.Ci, corresponding to blood doses of 5-8 Gy. Addnl. bone marrow transplantation allowed for an increase of the MTD of 90Y-Fab' to 400 .mu.Ci and for 213Bi-Fab' to 1100 .mu.Ci, resp. At these very dose levels, no biochem. or histol. evidence of **renal** damage was obsd. (**kidney** doses of <35 Gy).
At equitoxic dosing, 213Bi-labeled Fab' fragments were significantly more effective than the resp. 90Y-labeled conjugates. In the metastatic model, all untreated controls died from rapidly progressing hepatic metastases at 6-8 wk after tumor inoculation, whereas a histol. confirmed cure was obsd. in 95% of those animals treated with 700 .mu.Ci of 213Bi-Fab' 10 days after model induction, which is in contrast to an only 20% cure rate in mice treated with 250 .mu.Ci of 90Y-Fab'. These data show that RIT with .alpha. emitters may be therapeutically more effective than conventional .beta. emitters. Surprisingly, max. tolerated blood doses were, at 5-8 Gy, very similar between high-LET .alpha. and low-LET .beta. emitters. Due to its short phys. half-life, 213Bi appears to be esp. suitable for use in conjunction with fast-clearing fragments.

L42 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:226245 CAPLUS

TITLE: 90Y dosimetry in the nude mouse: evaluation of three dosimetry models in relation to the observed biological effects in the radioimmunotherapy of human colon cancer xenografts

AUTHOR(S): **Behr, T. M.**; Sgouros, G.; Sharkey, R. M.; Dunn, R. M.; Blumenthal, R. D.; Kolbert, K.; Juweid, M. E.; Siegel, J. A.; **Goldenberg, D. M.**

CORPORATE SOURCE: Garden State Cancer Center at the Center for Molecular Medicine and Immunology, Newark, NJ, 07103, USA

SOURCE: Int. Radiopharm. Dosim. Symp., Proc. Conf., 6th (1999), Volume 1, 257-271. Editor(s): Schlafke-Stelson, Audrey T.; Stabin, Michael G.; Sparks, Richard B. National Technical Information Service: Springfield, Va. CODEN: 68TXAO

DOCUMENT TYPE: Conference

LANGUAGE: English

AB Due to the long path length of high-energy .beta.-emitters, cross-organ radiation may become an important issue in small animal models. The aim of this study, therefore, was to evaluate three different dosimetry models in relation to obsd. biol. effects in radioimmunotherapy (RAIT) with 90Y-labeled immunoconjugates (IgG, F(ab)2 and Fab) in nude mice. The max. tolerated dose (MTD) of the 90Y-labeled anti-CEA MAb MN-14 (Fab, F(ab)2, and IgG), as well as the dose-limiting organ toxicities were detd. in GW-39 colon cancer xenografted nude mice (s.c. or metastatic). The mice were treated without artificial support, with inhibition of the **renal** uptake of antibody fragments by **D-lysine** (1,2), with bone marrow transplantation (BMT), or with combinations of each. Blood counts, **kidney** and liver function parameters, histol., and tumor growth were monitored. The 90Y dosimetry was calcd. based on three different model assumptions: 1) taking only self-doses into account, using S factors for spheres (3); 2) correcting for cross-organ irradn. according to the model of Hui et al. (4); and 3) using actual mouse anatomy as represented by magnetic resonance imaging (MRI) with a three-dimensional internal dosimetry package (3D-ID) developed by Sgouros et al. (5). Self-doses of Model 1 were not sufficient to describe the obsd. biol. effects, esp. near organs with a high activity accretion. With Fab, rising liver enzymes were obsd. at injected activities .gtoreq. 12 MBq, not explained by a self-dose of 4.3 Gy. Model 2 shows crossfire from the **kidneys**, resulting in an av. liver dose of 2.45 Gy/MBq. With F(ab)2 fragments, only the combination of BMT and lysine increased the MTD, explained by cross-organ radiation from the **kidneys** to the red marrow of the lumbar spine, described only by Model 3 (marrow self-dose

.ltoreq. 5 Gy, crossfire up to 0.8 Gy/MBq). Antitumor effects correlated well with calcd. doses. These data show that for understanding the biol. effects of 90Y in a mouse model, accounting for cross-organ irradn. is mandatory. The best correlation between biol. effects and the dosimetry was obtained by the third, MRI-anatomy-based model, which also allows the description of crossfire from abdominal organs to the red marrow.

L42 ANSWER 3 OF 11 USPATFULL
ACCESSION NUMBER: 1998:150898 USPATFULL
TITLE: Methods for reduced **renal** uptake of antibody fragments
INVENTOR(S): **Behr, Thomas M.**, Bloomfield, NJ, United States
Goldenberg, David M., Mendham, NJ, United States
PATENT ASSIGNEE(S): Center for Molecular Medicine and Immunology, Belleville, NJ, United States (U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 5843894	19981201	
APPLICATION INFO.:	US 1995-407899	19950321	(8)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Huff, Sheela
ASSISTANT EXAMINER: Reeves, Julie E.
LEGAL REPRESENTATIVE: Foley & Lardner
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Figure(s); 7 Drawing Page(s)
LINE COUNT: 825
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB **Kidney** uptake of antibody fragment conjugates in patients is reduced by administration to the patient of one or more compounds selected from the group consisting of **D-lysine**, poly-**D-lysine**, or poly-**L-lysine**, or pharmaceutically acceptable salts or carboxyl derivatives thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L42 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 2
ACCESSION NUMBER: 1998:491847 CAPLUS
DOCUMENT NUMBER: 129:257050
TITLE: Experimental studies on the role of antibody fragments in cancer radio-immunotherapy: influence of radiation dose and dose rate on toxicity and anti-tumor efficacy
AUTHOR(S): **Behr, Thomas M.**; Memtsoudis, Stavros;

Searcher : Shears 308-4994

Sharkey, Robert M.; Blumenthal, Rosalyn D.; Dunn, Robert M.; Gratz, Stefan; Wieland, Eberhard; Nebendahl, Klaus; Schmidberger, Heinz; **Goldenberg, David M.**; Becker, Wolfgang
CORPORATE SOURCE: Department of Nuclear Medicine, Georg-August-University, Gottingen, Germany
SOURCE: Int. J. Cancer (1998), 77(5), 787-795
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Whereas bivalent fragments have been widely used for radio-immunotherapy, no systematic study has been published on the therapeutic performance of monovalent conjugates in vivo. The aim of our study was, therefore, to det. the therapeutic performance of 131I-labeled Fab as compared to bivalent conjugates and to analyze factors that influence dose-limiting organ toxicity and anti-tumor efficacy. The max. tolerated doses (MTDs) and dose-limiting organ toxicities of the 131I-labeled anti-CEA antibody MN-14 [IgG, F(ab')2 and Fab] were detd. in nude mice bearing s.c. human colon cancer xenografts. Mice were treated with or without bone marrow transplantation (BMT) or inhibition of the **renal** accretion of antibody fragments by **D-lysine** or combinations thereof. Toxicity and tumor growth were monitored. Radiation dosimetry was calcd. from biodistribution data. With all 3 131I-labeled immunoconjugates [IgG, F(ab')2 and Fab], the red marrow was the only dose-limiting organ; MTDs were 260 .mu.Ci for IgG, 1,200 .mu.Ci for F(ab')2 and 3 .mu.Ci for Fab, corresponding to blood doses of 17 Gy, 9 Gy and 4 Gy, resp. However, initial dose rates were 10 times higher with Fab as compared to IgG and 3 times higher as compared to F(ab')2. The MTD of all 3 immunoconjugates was increased by BMT by approx. 30%. In accordance with **renal** doses below 10 Gy, no signs of nephrotoxicity were obsd. Despite lower absorbed tumor doses, at equitoxic dosing, Fab fragments were more effective at controlling tumor growth than the resp. bivalent fragment or IgG, probably due to higher intratumoral dose rates. Our data indicate that the improved anti-tumor effectiveness of antibody fragments as compared to IgG and the higher myelotoxicity at comparably lower red marrow doses are most likely due to the higher initial dose rates obsd. with antibody fragments.

L42 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 3
ACCESSION NUMBER: 1998:678097 CAPLUS
DOCUMENT NUMBER: 130:49277
TITLE: 90Yttrium-Labeled Complementarity-Determining-Region-Grafted Monoclonal Antibodies for Radioimmunotherapy: Radiolabeling and Animal Biodistribution Studies
Searcher : Shears 308-4994

AUTHOR(S): Govindan, Serengulam V.; Shih, Lisa B.; **Goldenberg, David M.**; Sharkey, Robert M.; Karacay, Habibe; Donnelly, Joseph E.; Losman, Michele J.; Hansen, Hans J.; Griffiths, Gary L.
CORPORATE SOURCE: Immunomedics Inc., Morris Plains, NJ, 07950, USA
SOURCE: Bioconjugate Chem. (1998), 9(6), 773-782
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 90Yttrium-labeled monoclonal antibodies (mAbs) are likely to be important to radioimmunotherapy (RAIT) of a variety of cancers. The goal of this study was to select and evaluate a form of [90Y]mAb suitable for RAIT and det. conditions for high-yield, reproducible radiolabelings. 90Y-Labelings, at 2-40 mCi levels, of cdr-grafted versions of anti-B-cell lymphoma (hLL2) and anti-CEA (hIMMU-14) mAbs were optimized to >90% incorporations using the macrocyclic chelator DOTA as the metal carrier. In in vitro challenge assays, the stability of mAbs labeled with [90Y]DOTA was better than that of the corresponding [90Y]benzyl-DTPA conjugates. The retention of [90Y]DOTA-hLL2 on Raji tumor cells in vitro was similar to that of the same mAb labeled with [90Y]benzyl-DTPA and was about twice as much as with [125I]hLL2, indicating residualization of metalated mAb. Both [90Y]hLL2 conjugates, prepd. using DOTA and Bz-DTPA, had similar max. tolerated doses of 125 .mu.Ci in BALB/c mice and showed no discernible chelator-induced immune responses. Animal biodistribution studies in nude mice bearing Ramos human B-cell lymphoma xenografts revealed similar tumor and tissue uptake over a 10 day period, with the exception of bone uptake which was up to 50% lower for [88Y]DOTA-hLL2 compared to [88Y]Bz-DTPA-hLL2 at time points beyond 24 h. With [90Y]DOTA-hLL2 fragments, in vivo animal tumor dosimetries were inferior to those for the IgG, and **kidney** uptake was relatively high even with **D-lysine** administration. The ability of [111In]DOTA-hLL2 to accurately predict [90Y]DOTA-hLL2 biodistribution was established. These preclin. findings demonstrate that [90Y]DOTA-(CDR-grafted) mAbs are suitable for examn. in clin. RAIT.

L42 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 4
ACCESSION NUMBER: 1998:12681 CAPLUS
DOCUMENT NUMBER: 128:125381
TITLE: Overcoming the nephrotoxicity of radiometal-labeled immunoconjugates: improved cancer therapy administered to a nude mouse model in relation to the internal radiation dosimetry
AUTHOR(S): **Behr, Thomas M.**; Sharkey, Robert M.; Sgouros, George; Blumenthal, Rosalyn D.; Dunn,

Robert M.; Kolbert, Katherine; Griffiths, Gary L.; Siegel, Jeffry A.; Becker, Wolfgang S.; **Goldenberg, David M.**

CORPORATE SOURCE: Garden State Cancer Center at the Center for Molecular Medicine and Immunology, Belleville, NJ, 07109, USA

SOURCE: Cancer (N. Y.) (1997), 80(12, Suppl.), 2591-2610
CODEN: CANCAR; ISSN: 0008-543X

PUBLISHER: John Wiley & Sons, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Elevated **renal** uptake and extended retention of radiolabeled antibody fragments and peptides is a problem in the therapeutic application of such agents. However, cationic amino acids have been shown to reduce **renal** accretion. The aims of the current study were to evaluate whether this methodol. would benefit therapy with yttrium 90 (90Y)-labeled antibody fragments (Fab, F(ab)2), to establish the relationship between radiation dosimetry and obsd. biol. effects, and to compare the antitumor efficacy of antibody fragments with that of whole Ig (Ig)G. The max. tolerated dose (MTD) and the dose-limiting organ toxicity of 90Y-labeled anti-carcinoembryonic antigen (CEA) MN-14 monoclonal antibodies (Fab, F(ab)2, and IgG) were detd. in nude mice bearing GW-39 human colon carcinoma xenografts. The mice were treated with or without **kidney** protection by administration of **D-lysine**, with or without bone marrow transplantation (BMT), or with combinations of each. Toxicity and tumor growth were monitored at weekly intervals after radioimmunotherapy. Dosimetry was calcd. from bio-distribution studies using 88Y-labeled antibody. Three different dosimetric models were examd.: 1) taking solely self-to-self doses into account, using S factors for 90Y in spheroids from 0.1 to 1 g; 2) correcting for cross -organ radiation; and 3) using actual mouse anatomy as represented by NMR imaging with a three-dimensional internal dosimetry package (3D-ID). The **kidney** was the first dose limiting organ with the use of Fab fragments. Acute radiation nephritis occurred at injected activities .gtoreq.325 .mu.Ci, and chronic nephrosis at doses .gtoreq.250 .mu.Ci. Activities of 200 .mu.Ci were tolerated by 100% of the animals (i.e., the MTD). Application of lysine decreased the **renal** dose by approx. fivefold, facilitating a 25% increase in the MTD (to 250 .mu.Ci), because myelotoxicity became dose-limiting despite red marrow doses of less than 5 Gy (Gy). By using BMT and lysine, the MTD could be doubled from 200 to 400 .mu.Ci, where no biochem. or histol. evidence of **renal** damage was obsd. (**kidney** dose, .ltoreq.40 Gy). With injected activities of .gtoreq. 325.mu.Ci without **kidney** protection, and with a hepatic self-to-self dose of only 4 Gy, rising liver enzymes were obsd., which could be explained only by cross-organ radiation from

radioactivity in the **kidneys** (in the immediate neighborhood of the right **kidney** up to .gtoreq. 150 Gy). The MTD of F(ab)2 fragments could be elevated only by a combination of BMT and lysine. With IgG, the bone marrow alone was dose-limiting. Tumor dosimetry correlated well with antitumor effects; Fab was more effective than F(ab)2, which was consistent with its more favorable dosimetry, and it may also be more effective than IgG due to its higher dose rate and more homogenous distribution. Dosimetry Model 1 was insufficient for predicting biol. effects. Model 2 seemed to be more accurate, accounting for interorgan crossfire. However, Model 3 showed an addnl. substantial contribution to the red bone marrow dose due to crossfire from the abdominal organs. These data show that radiation nephrotoxicity is an important effect of cancer therapy with radiometal-conjugated antibody fragments or peptides. However, this effect can be overcome successfully with the application of cationic amino acids, which substantially increase the anti-tumor efficacy of radiometal-labeled immunoconjugates. For understanding the biol. effects (e.g., liver toxicity) of 90Y in a mouse model, accounting for cross-organ radiation is essential. Further studies with radiometal conjugated monoclonal antibody fragments and peptides are necessary to det. the MTD, dose-limiting organs, antitumor effectiveness, and nephroprotective effects of cationic amino acids in humans.

L42 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 5

ACCESSION NUMBER: 1996:681542 CAPLUS
DOCUMENT NUMBER: 125:317395
TITLE: Lysine and polylysine for reduced **renal** uptake of antibody fragments
INVENTOR(S): **Behr, Thomas M.; Goldenberg, David M.**
PATENT ASSIGNEE(S): Center for Molecular Medicine and Immunology, USA
SOURCE: PCT Int. Appl., 37 pp
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9629087	A1	19960926	WO 1996-US3308	19960320

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB,

GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML

US 5843894	A	19981201	US 1995-407899	19950321
CA 2190867	AA	19960926	CA 1996-2190867	19960320
AU 9653616	A1	19961008	AU 1996-53616	19960320
AU 700346	B2	19990107		
EP 767673	A1	19970416	EP 1996-910422	19960320
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10505866	T2	19980609	JP 1996-528465	19960320
PRIORITY APPLN. INFO.:			US 1995-407899	19950321
			WO 1996-US3308	19960320

AB **Kidney** uptake of antibody fragment conjugates in patients undergoing radioimmunodiagnosis, immunotherapy, or radioimmunotherapy is reduced by administration of the patient of one or more compds. selected from the group consisting of lysine and/or polylysine, pharmaceutically acceptable salts or carboxyl derivs. thereof. Human patients undergoing radioimmunodetection with 99mTc-labeled Fab' fragments of two anti-carcinoembryonic antigen antibodies were infused over a 3-h period with a com. amino acid soln. contg. 1.75 g **L-lysine**. A decrease of **kidney** uptake of radiolabeled fragments was obsd., the effect being more pronounced at 24 h than at 4 h post injection. However, poly(**L-lysine**) with a mol. wt. of 1-4 kDa reduced **kidney** uptake with a single i.p. injection at lower doses than the monomer. The potency of poly(**L-lysine**) increased with increasing mol. wt.

L42 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1996:343819 CAPLUS
DOCUMENT NUMBER: 125:29193
TITLE: Reduction of **renal** uptake of monoclonal antibody fragments by amino acid infusion
AUTHOR(S): **Behr, Thomas M.**; Becker, Wolfgang S.; Sharkey, Robert M.; Juweid, Malik E.; Dunn, Robert M.; Bair, Hans-J.; Wolf, Friedrich G.; **Goldenberg, David M.**
CORPORATE SOURCE: Garden State Cancer Center, Center for Molecular Medieine and Immunology, Newark, NJ, 07103-2763, USA
SOURCE: J. Nucl. Med. (1996), 37(5), 829-833
CODEN: JNMEAQ; ISSN: 0161-5505
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The **renal** uptake of radiolabeled antibody fragments and peptides presents a problem in radioimmunodetection and therapy, compromising lesion sensitivity, esp. with intracellularly-retained isotopes. Previously, we showed that cationic amino acids and their

derivs. are capable of significantly reducing **kidn y** uptake in animals. We report our initial clin. results of successful **renal** uptake redn. in five patients who underwent cancer radioimmunodetection with 99mTc-anti-CEA Fab' fragments. The patients were infused with two liters of a com.-available nutritive amino acid soln. (contg. approx. 2.25 g/ **L lysine**-glutamate and 2.50 g/L arginine), whereas 75 control patients received the same vol. of saline (quantification of organ and tumor kinetics from conjugate whole-body views by ROI technique). The **renal** uptake in the amino acid group was significantly lower ($p < 0.05$) than in the control group (11.1% injected dose vs. 17.7% injected dose at 24 h postinjection), whereas the uptake of all other organs remained unaffected. Gel filtration chromatog. of the urine taken from amino-acid-treated patients showed that a significantly higher amt. of excreted activity was bound to intact Fab' (53% of excreted activity) in contrast to only less than 10% in the control group. The **renal** uptake of monoclonal antibody fragments in patients can be reduced significantly by amino acid infusion, even at considerably lower doses than those that were safe and effective in animals. As was found in animals, the mechanism seems to rely on an inhibition of the re-absorption of tubularly-filtered proteins by the proximal tubule cells. These results encourage further clin. trials to lower the **renal** uptake experienced in radioimmunodetection, as well as in therapeutic trials with antibody fragments and peptides.

L42 ANSWER 9 OF 11 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 95368640 MEDLINE
DOCUMENT NUMBER: 95368640
TITLE: Reduction of the **renal** uptake of radiolabeled monoclonal antibody fragments by cationic amino acids and their derivatives.
AUTHOR: **Behr T M**; Sharkey R M; Juweid M E; Blumenthal R D; Dunn R M; Griffiths G L; Bair H J; Wolf F G; Becker W S; **Goldenberg D M**
CORPORATE SOURCE: Garden State Cancer Center, Center for Molecular Medicine and Immunology, Newark, New Jersey 07103-2763, USA.
CONTRACT NUMBER: CA39841 (NCI)
SOURCE: CANCER RESEARCH, (1995 Sep 1) 55 (17) 3825-34. Journal code: CNF. ISSN: 0008-5472.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199511
AB The **renal** uptake of radiolabeled antibody fragments and peptides is a problem in radioimmunodetection and

radioimmunotherapy, especially with intracellular retained radiometals. The aim of this study was to develop suitable methods to reduce this **kidney** uptake. BALB/c mice or nude mice bearing the human GW-39 colon carcinoma xenograft were given i.p. injections of basic amino acids or a range of different basic amino acid derivatives, amino sugars, as well as cationic peptides. The effect of these agents on the biodistribution of Fab' and F(ab')2 fragments of different mAbs radiolabeled with 99mTc, 188Re, 111In, 88Y, or 125I was studied. Tumor and organ uptake was determined and compared to untreated mice. The **kidney** uptake of Fab' fragments was reduced 5-6-fold in a dose-dependent manner as compared to untreated controls. The uptake in all other organs, as well as the tumor, was unaffected. A similar reduction in **renal** retention was seen for all other intracellularly retained isotopes, as well as for F(ab')2 fragments. D- and L-isomers of lysine were equally effective whether given i.p. or p.o. D-glucosamine was effective, but its N-acetyl derivative was not. Basic polypeptides (e.g., poly-**L-lysine**) were also effective; their potency increased with increasing molecular weight. HPLC of the urine taken from treated animals showed the excretion of intact Fab', in contrast to mostly low-molecular-weight metabolites in the control group. These studies indicate that a variety of basic compounds is capable of inhibiting the tubular reabsorption of peptides and proteins, thus lowering the **kidney** uptake of antibody fragments significantly. On a molecular basis, the effect seems to essentially rely on the presence of a positively charged amino group. By reducing **renal** retention of antibody fragments, their role as imaging and therapeutic agents may be expanded.

L42 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1995:783642 CAPLUS
DOCUMENT NUMBER: 123:221932
TITLE: Reduction of the **renal** uptake of radiolabeled monoclonal antibody fragments by cationic amino acids and their derivatives
AUTHOR(S): **Behr, Thomas M.**; Sharkey, Robert M.; Juweid, Malik E.; Blumenthal, Rosalyn D.; Dunn, Robert M.; Griffiths, Gary L.; Bair, Hans-J.; Wolf, Friedrich G.; Becker, Wolfgang S.; **Goldenberg, David M.**
CORPORATE SOURCE: Garden State Cancer Cent. Cent. Mol. Med. Immunol., Newark, NJ, 07103-2763, USA
SOURCE: Cancer Res. (1995), 55(17), 3824-34
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **renal** uptake of radiolabeled antibody fragments and peptides is a problem in radioimmunodetection and

radioimmunotherapy, esp. with intracellularly retained radiometals. The aim of this study was to develop suitable methods to reduce this **kidney** uptake. BALB/c mice or nude mice bearing the human GW-39 colon carcinoma xenograft were given i.p. injections of basic amino acids or a range of different basic amino acid derivs., amino sugars, as well as cationic peptides. The effect of these agents on the biodistribution of Fab' and F(ab')2 fragments of different mAbs radiolabeled with 99mTc, 188Re, 111In, 88Y, or 125I was studied. Tumor and organ uptake was detd. and compared to untreated mice. The **kidney** uptake of Fab' fragments was reduced 5-6-fold in a dose-dependent manner as compared to untreated controls. The uptake in all other organs, as well as tumor, was unaffected. A similar redn. in **renal** retention was seen for all other intracellularly retained isotopes, as well as for F(ab')2 fragments. D- And L-isomers of lysine were equally effective whether given i.p. or p.o. D-Glucosamine was effective, but its N-acetyl derivs. was not. Basic polypeptides (e.g., poly-**L-lysine**) were also effective; their potency increased with increasing mol. wt. HPLC of the urine taken from treated animals showed the excretion of intact Fab', in contrast to mostly low-mol.-wt. metabolites in the control group. These studies indicate that a variety of basic compds. is capable of inhibiting the tubular resorption of peptides and proteins, thus lowering the **kidney** uptake of antibody fragments significantly. On a mol. basis, the effect seems to essentially rely on the presence of a pos. charged amino group. By reducing **renal** retention of antibody fragments, their role as imaging and therapeutic agents may be expanded.

L42 ANSWER 11 OF 11 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1995:187844 BIOSIS
DOCUMENT NUMBER: PREV199598202144
TITLE: Reduction of **kidney** uptake of Fab' fragments of monoclonal antibodies: Animal experiments and initial clinical results.
AUTHOR(S): **Behr, T. M.**; Sharkey, R. M.; Juweid, M. E.; Aninipot, R.; **Goldenberg, D. M.**
CORPORATE SOURCE: Garden State Cancer Cent., Newark, NJ 07103 USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (1995) Vol. 36, No. 0, pp. 617.
Meeting Info.: Eighty-sixth Annual Meeting of the American Association for Cancer Research Toronto, Ontario, Canada March 18-22, 1995
ISSN: 0197-016X.
DOCUMENT TYPE: Conference
LANGUAGE: English

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L11 ANSWER 16 OF 19 JICST-EPlus COPYRIGHT 2000 JST
ACCESSION NUMBER: 940939922 JICST-EPlus
TITLE: Reabsorption of proteins in renal tubules.
AUTHOR: KUDO SHOJI; GOTO HIROHIKO; ODOMI MASAAKI
CORPORATE SOURCE: Otsuka Pharm. Co., Ltd., Tokushima Res. Inst.
SOURCE: Yakubutsu Dotai (Xenobiotic Metabolism and Disposition), (1994) vol. 9, no. Suppl, pp. S114-S117. Journal Code: X0758A (Fig. 1, Tbl. 1, Ref. 4)
CODEN: YADOEL; ISSN: 0916-1139
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
LANGUAGE: Japanese
STATUS: New

AB In order to investigate the mechanism of the reabsorption of a protein in renal tubules of rats, we employed OCT-7000, which is a recombinant variant of natiral human interleukin-1.ALPHA. with a molecular mass of approximately 18,000. In this study, OCT-7000 **uptake** in **renal** tubules was examined using immunoelectron microscopic technique with immunogold staining. The effects of various proteins or synthetic polypeptides on the urinary excretion of OCT-7000 were also investigated. Immunoelectron microscopic observations showed that OCT-7000 was taken up into the endocytic vesicle close to the brush border membrane located in segment 2 of the proximal tubules, followed by accumulation of secondary lysosmes. Urinary excretion of OCT-7000 after systemic **administration** was extremely low, accounting for 0.014% of the dose. Human serum albumin had no effect on the excretion of OCT-7000, while increases in the urinary excretion of OCT-7000 were found in rats treated with a trypsin inhibitor, myoglobin and trypsinogen, in a dose-dependent manner. The order of potency for urinary excretion of OCT-7000 was trypsinogen>myoglobin>trypsin inhibitor. Poly-**L-lysine**, a synthetic polypeptide dose-dependently increased the urinary excretion of OCT-7000, whereas poly-L-glutamic acid had no effect on excretion. Specifically, the data reveal that reabsorption of OCT-7000 in the proximal tubules was inhibited by trypsinogen, myoglobin, trypsin inhibitor or poly-**L-lysine**, resulting in an increase of urinary excretion of OCT-7000. Furthermore, it was considered that negative charges on the brush border membrane in the proximal tubules were involved in the reabsorption of OCT-7000 because the inhibitory potency of proteins or synthetic polypeptides on the reabsorption of OCT-7000 was increased with a high isoelectric point. From the above, the mechanisms of reabsorption of protein in renal tubule are speculated as follows. (abridged author abst.)

L11 ANSWER 17 OF 19 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 93160295 MEDLINE
DOCUMENT NUMBER: 93160295
TITLE: Copolymers of lysine and polyethylene glycol: a new family of functionalized drug carriers [published erratum appears in Bioconjug Chem 1993 Sep-Oct;4(5):410].
AUTHOR: Nathan A; Zalipsky S; Ertel S I; Agathos S N; Yarmush M L; Kohn J
CORPORATE SOURCE: Department of Chemistry, Rutgers-State University of New Jersey, New Brunswick 08903..
CONTRACT NUMBER: GM00550 (NIGMS)
SOURCE: BIOCONJUGATE CHEMISTRY, (1993 Jan-Feb) 4 (1) 54-62. Journal code: A1T. ISSN: 1043-1802.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199305

AB Poly(PEG-Lys), a new, water-soluble poly(ether urethane), derived from **L-lysine** and poly(ethylene glycol) was investigated as a precursor for the preparation of polymeric drug conjugates. To facilitate a wide variety of coupling chemistries, the pendent carboxyl groups of poly(PEG-Lys) were converted to other reactive functional groups (amino, hydroxyl, active ester, and aldehyde) in high yield. These reactive pendent chains were then used as anchors for the covalent attachment of penicillin V and cephradine, two clinically used antimicrobial agents. Coupling to the carrier was achieved in good yields and the chemical versatility of this system was demonstrated by the preparation of conjugates having antibiotic ligands linked via biostable or biodegradable linkages to the carrier, either directly or via a spacer. Conjugate 4, poly(PEG-Lys-penicillin V ester), was obtained by linking penicillin V to the polymer backbone via hydrolytically labile ester bonds. This conjugate exhibited activity similar to that of the parent drug against three clinically important strains of bacteria. Drug activity coincided with the release of the drug from the carrier. Hydrolytically stable cephradine-containing conjugates were prepared by three different coupling methods but showed no antibiotic activity. 14C-labeled poly(PEG-Lys) was injected into mice and its biodistribution was monitored for 48 h. The carrier showed no preferential **uptake** by liver, spleen, or **kidney**. No signs of acute toxicity were evident in mice or rats when poly(PEG-Lys) was **administered** iv and ip at doses up to 10 g/kg. These results indicate that poly(PEG-Lys) is a promising precursor for the preparation of soluble drug conjugates.

L11 ANSWER 18 OF 19 MEDLINE
ACCESSION NUMBER: 89252711 MEDLINE

DOCUMENT NUMBER: 89252711
TITLE: Transport of nutrients into the renal brush border membrane vesicles as marker in evaluating the role of antipili antibodies in modulation of ascending pyelonephritis in rats.
AUTHOR: Garg U C; Ganguly N K; Sharma S; Bhatnagar R
CORPORATE SOURCE: Department of Experimental Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, India..
SOURCE: FEMS MICROBIOLOGY LETTERS, (1989 Jan 15) 48 (2) 155-9.
Journal code: FML. ISSN: 0378-1097.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198909

AB The uptake of D-glucose, L-aspartate, **L-lysine** and L-proline was investigated in renal brush border membrane (BBM) vesicles prepared from control, infected or passively-immunized-infected rats. Except L-aspartate, a progressive decrease in the uptake of these nutrients in both infected and immunized-infected groups during the course of infection was observed, but the changes were less apparent in immunized-infected rats than in non-immunized ones. The uptake of L-aspartate was increased in vesicles from early stages of infection but decreased in those from later stages. Also in L-aspartate uptake, the changes were smaller in immunized animals. The uptake of nutrients was detectable earlier than were histopathological alterations of both **kidneys**. The observations demonstrated that **uptake** of D-glucose and amino acids in the kidneys is disturbed prior to appearance of histopathological lesions and thus can be used for early detection of the disease. The data also demonstrate that antipili antibodies afford partial protection against ascending pyelonephritis.

L11 ANSWER 19 OF 19 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 74034343 EMBASE
DOCUMENT NUMBER: 1974034343
TITLE: **L lysine uptake** in rat **kidney** cortex slices treated with diazene dicarboxylic acid bis (N,N dimethylamide).
AUTHOR: Hewitt J.; Leibach F.
CORPORATE SOURCE: Dept. Cell Molec. Biol., Med. Coll. Georgia, Augusta, Ga. 30902, United States
SOURCE: Federation Proceedings, (1973) 32/3 (I) (4082).
CODEN: FEPRA7
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
LANGUAGE: English

Searcher : Shears 308-4994

(FILE 'USPATFULL' ENTERED AT 10:07:58 ON 09 MAY 2000)
L13 37 SEA ABB=ON PLU=ON (L3 OR (L OR D)(W)(LYSINE OR LYS))(L)((KIDNEY OR RENAL?)(5A)(UPTAK? OR RETENT?))
L14 28 SEA ABB=ON PLU=ON L13(L)ADMIN?

L14 ANSWER 1 OF 28 USPATFULL
ACCESSION NUMBER: 2000:15742 USPATFULL
TITLE: Pretargeting methods and compounds
INVENTOR(S): Gustavson, Linda M., Seattle, WA, United States
Theodore, Louis J., Lynnwood, WA, United States
Su, Fu-Min, Seattle, WA, United States
Reno, John M., Brier, WA, United States
PATENT ASSIGNEE(S): NeoRx Corporation, Seattle, WA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6022966	20000208
APPLICATION INFO.:	US 1993-156565	19931122 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. WO 1993-US5406, filed on 7 Jun 1993, now patented, Pat. No. WO 5608060 which is a continuation-in-part of Ser. No. US 1992-995381, filed on 23 Dec 1992, now abandoned which is a continuation-in-part of Ser. No. US 1992-895588, filed on 9 Jun 1992, now patented, Pat. No. US 5283342
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Cunningham, Thomas M.
LEGAL REPRESENTATIVE: Seed and Berry LLP
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Figure(s); 12 Drawing Page(s)
LINE COUNT: 4010
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods, compounds, compositions and kits that relate to pretargeted delivery of diagnostic and therapeutic agents are disclosed. In particular, methods for radiometal labeling of biotin, as well as related compounds, are described. Articles of manufacture useful in pretargeting methods are also discussed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 540/474.000
INCLS: 548/304.100; 536/001.110
NCL NCLM: 540/474.000
NCLS: 536/001.110; 548/304.100

L14 ANSWER 2 OF 28 USPATFULL
ACCESSION NUMBER: 2000:7398 USPATFULL
Searcher : Shears 308-4994

TITLE: Biotinamido-n-methylglycyl-seryl-o-succinamido-benzyl dota

INVENTOR(S): Theodore, Louis J., Lynnwood, WA, United States
Kasina, Sudhakar, Kirkland, WA, United States
Reno, John M., Brier, WA, United States
Gustavson, Linda M., Seattle, WA, United States

PATENT ASSIGNEE(S): NeoRx Corporation, Seattle, WA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6015897	20000118
APPLICATION INFO.:	US 1996-645211	19960513 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1994-351005, filed on 7 Dec 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-163188, filed on 7 Dec 1993, now abandoned which is a continuation-in-part of Ser. No. WO 1993-US5406, filed on 7 Jun 1993 which is a continuation-in-part of Ser. No. US 1992-995381, filed on 23 Dec 1992, now abandoned which is a continuation-in-part of Ser. No. US 1992-895588, filed on 9 Jun 1992, now patented, Pat. No. US 5283342

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Chan, Christina Y.
ASSISTANT EXAMINER: Gambel, Phillip
LEGAL REPRESENTATIVE: Seed and Berry LLP
NUMBER OF CLAIMS: 1
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 12 Drawing Figure(s); 7 Drawing Page(s)
LINE COUNT: 6303
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods, compounds, compositions and kits that relate to pretargeted delivery of diagnostic and therapeutic agents are disclosed. Biotinamido-N-methylglycyl-seryl-O-succinamido-benzyl DOTA is disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 540/474.000
NCL NCLM: 540/474.000

L14 ANSWER 3 OF 28 USPATFULL
ACCESSION NUMBER: 2000:1524 USPATFULL
TITLE: Biodegradable blood-pool contrast agents
INVENTOR(S): Margerum, Larry, Wayne, PA, United States
Campion, Brian, Solano Beach, CA, United States
Fellmann, Jere Douglas, Livermore, CA, United States

Searcher : Shears 308-4994

	Garrity, Martha, San Clemente, CA, United States
	Varadarajan, John, Sunnyvale, CA, United States
PATENT ASSIGNEE(S):	Nycomed Salutar, Inc., Wayne, PA, United States (U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 6010681	20000104	
	WO 9528967	19951102	
APPLICATION INFO.:	US 1997-722080	19970121	(8)
	WO 1995-GB899	19950420	
		19970121	PCT 371 date
		19970121	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1994-7812	19940420
	GB 1994-20657	19941013

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Hollinden, Gary E.
LEGAL REPRESENTATIVE: Fish & Richardson P.C.
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
LINE COUNT: 1469

AB The invention provides a blood pool contrast agent having an overall molecular weight of at least 10KD comprising a macrostructure which has bound thereto a plurality of opsonization inhibiting moieties and carries chelated ionic paramagnetic or heavy metal moieties, the chelant groups for said chelated moieties being macrocyclic where said macrostructure is liposomal.

INCL INCLM: 424/009.350
INCLS: 424/009.360; 424/009.364; 424/009.420
NCL NCLM: 424/009.350
NCLS: 424/009.360; 424/009.364; 424/009.420

L14 ANSWER 4 OF 28 USPATFULL
ACCESSION NUMBER: 1999:136685 USPATFULL
TITLE: Pretargeting protocols for the enhanced localization of cytotoxins to target sites and cytotoxic combinations useful therefore
INVENTOR(S): Fritzberg, Alan R., Edmonds, WA, United States
Abrams, Paul G., Seattle, WA, United States
Reno, John M., Brier, WA, United States
Axworthy, Donald B., Brier, WA, United States
Graves, Scott S., Monroe, WA, United States
Kasina, Sudhakar, Kirkland, WA, United States
PATENT ASSIGNEE(S): NeoRx Corporation, Seattle, WA, United States (U.S. corporation)

Searcher : Shears 308-4994

	NUMBER	DATE
PATENT INFORMATION:	US 5976535	19991102
APPLICATION INFO.:	US 1995-468513	19950606 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1993-163188, filed on 7 Dec 1993, now abandoned which is a continuation-in-part of Ser. No. WO 1993-US5406, filed on 7 Jun 1993 which is a continuation-in-part of Ser. No. US 1992-995381, filed on 23 Dec 1992, now abandoned which is a continuation-in-part of Ser. No. US 1992-895588, filed on 9 Jun 1992, now patented, Pat. No. US 5288342

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Cunningham, Thomas M.
LEGAL REPRESENTATIVE: Seed and Berry LLP
NUMBER OF CLAIMS: 3
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 13 Drawing Figure(s); 13 Drawing Page(s)
LINE COUNT: 4278
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods for targeting cytotoxins to target sites by administration of a combination of conjugates are provided. Novel cytotoxic combinations for use in such methods are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/182.100
INCLS: 424/178.100; 530/387.300; 530/388.800; 530/391.700
NCL NCLM: 424/182.100
NCLS: 424/178.100; 530/387.300; 530/388.800; 530/391.700

L14 ANSWER 5 OF 28 USPATFULL
ACCESSION NUMBER: 1999:113890 USPATFULL
TITLE: Biotinidase resistant biotin-DOTA conjugates
INVENTOR(S): Axworthy, Donald B., Brier, WA, United States
Theodore, Louis J., Lynnwood, WA, United States
Gustavson, Linda M., Seattle, WA, United States
Reno, John M., Brier, WA, United States
PATENT ASSIGNEE(S): NeoRx Corporation, Seattle, WA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5955605	19990921
APPLICATION INFO.:	US 1996-695940	19960812 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1995-351469, filed on 21 Feb 1995, now patented, Pat. No. US 5608060

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Eisenschenk, Frank C.
LEGAL REPRESENTATIVE: Seed and Berry LLP
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 22 Drawing Figure(s); 24 Drawing Page(s)
LINE COUNT: 4727
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Biotinidase-resistant biotin-DOTA conjugates, and methods of use thereof in diagnostic and therapeutic pretargeting methods are provided. These conjugates are useful in diagnosis and treatment of cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 540/474.000
INCLS: 548/303.700; 548/304.100; 536/001.110; 536/017.400; 536/053.000; 424/009.363
NCL NCLM: 540/474.000
NCLS: 424/009.363; 536/001.110; 536/017.400; 536/053.000; 548/303.700; 548/304.100

L14 ANSWER 6 OF 28 USPATFULL
ACCESSION NUMBER: 1999:69701 USPATFULL
TITLE: Pretargeting methods and compounds
INVENTOR(S): Axworthy, Donald B., Brier, WA, United States
Fritzberg, Alan R., Edmonds, WA, United States
Sanderson, James A., Seattle, WA, United States
PATENT ASSIGNEE(S): NeoRx Corporation, Seattle, WA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5914312	19990622
APPLICATION INFO.:	US 1994-297429	19940826 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1992-995383, filed on 23 Dec 1992, now abandoned which is a continuation-in-part of Ser. No. US 1992-895588, filed on 9 Jun 1992, now patented, Pat. No. US 5283342
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Eisenschenk, Frank C.
ASSISTANT EXAMINER: Nolan, Patrick
LEGAL REPRESENTATIVE: Seed and Berry LLP
NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 22 Drawing Figure(s); 22 Drawing Page(s)
LINE COUNT: 2191
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods, compounds, compositions and kits that relate to pretargeted delivery of diagnostic and therapeutic agents are

disclosed. In particular, methods for radiometal labeling of biotin and for improved radiohalogenation of biotin, as well as related compounds, are described. Also, clearing agents, anti-ligand-targeting moiety conjugates, target cell retention enhancing moieties and additional methods are discussed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/008.000
INCLS: 514/387.000; 530/363.000; 530/367.000; 530/350.000; 530/395.000; 530/394.000; 568/852.000; 536/112.000; 548/303.700
NCL NCLM: 514/008.000
NCLS: 514/387.000; 530/350.000; 530/363.000; 530/367.000; 530/394.000; 530/395.000; 536/112.000; 548/303.700; 568/852.000

L14 ANSWER 7 OF 28 USPATFULL
ACCESSION NUMBER: 1999:66990 USPATFULL
TITLE: Pretargeting protocols for enhanced localization of active agents to target sites
INVENTOR(S): Axworthy, Donald B., Brier, WA, United States
Mallett, Robert W., Seattle, WA, United States
Hylarides, Mark D., Mukilteo, WA, United States
Fritzberg, Alan R., Edmonds, WA, United States
PATENT ASSIGNEE(S): NeoRx Corporation, Seattle, WA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5911969	19990615
APPLICATION INFO.:	US 1994-329617	19941026 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1992-995381, filed on 23 Dec 1992, now abandoned which is a continuation-in-part of Ser. No. US 1992-895588, filed on 9 Jun 1992, now patented, Pat. No. US 5283342
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Eisenschenk, Frank C.
ASSISTANT EXAMINER: Nolan, Patrick J.
LEGAL REPRESENTATIVE: Seed and Berry LLP
NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 22 Drawing Figure(s); 22 Drawing Page(s)
LINE COUNT: 2172
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods, compounds, compositions and kits that relate to pretargeted delivery of diagnostic and therapeutic agents are disclosed. In particular, methods for radiometal labeling of biotin and for improved radiohalogenation of biotin, as well as

related compounds, are described. Also, clearing agents, anti-ligand-targeting moiety conjugates, target cell retention enhancing moieties and additional methods are discussed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/001.110
INCLS: 424/001.530; 424/001.450; 424/178.100; 424/181.100; 424/183.100; 424/179.100; 530/367.000; 530/350.000; 530/825.000; 530/391.900; 530/391.500; 514/387.000; 548/303.700
NCL NCLM: 424/001.110
NCLS: 424/001.450; 424/001.530; 424/178.100; 424/179.100; 424/181.100; 424/183.100; 514/387.000; 530/350.000; 530/367.000; 530/391.500; 530/391.900; 530/825.000; 548/303.700

L14 ANSWER 8 OF 28 USPATFULL
ACCESSION NUMBER: 1998:154419 USPATFULL
TITLE: Production of nitro-benzyl-dota via direct peptide cyclization
INVENTOR(S): Yau, Eric K., Kirkland, WA, United States
Theodore, Louis J., Lynnwood, WA, United States
Gustavson, Linda M., Seattle, WA, United States
PATENT ASSIGNEE(S): NeoRx Corporation, Seattle, WA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5847121	19981208
APPLICATION INFO.:	US 1995-571816	19951213 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1994-345811, filed on 22 Nov 1994, now patented, Pat. No. US 5541287 which is a continuation-in-part of Ser. No. US 1993-156565, filed on 22 Nov 1993 which is a continuation-in-part of Ser. No. US 1992-995381, filed on 23 Dec 1992, now abandoned which is a continuation-in-part of Ser. No. US 1992-895588, filed on 9 Jun 1992, now patented, Pat. No. US 5283342
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Datlow, Philip I.
LEGAL REPRESENTATIVE: Seed and Berry LLP
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1,6
NUMBER OF DRAWINGS: 16 Drawing Figure(s); 16 Drawing Page(s)
LINE COUNT: 4337
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods, compounds, compositions and kits that relate to pretargeted delivery of diagnostic and therapeutic agents are

disclosed. In particular, methods for radiometal labeling of biotin, as well as related compounds, are described. Articles of manufacture useful in pretargeting methods are also discussed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 540/474.000
NCL NCLM: 540/474.000

L14 ANSWER 9 OF 28 USPATFULL
ACCESSION NUMBER: 1998:150898 USPATFULL
TITLE: Methods for reduced renal uptake of antibody fragments
INVENTOR(S): Behr, Thomas M., Bloomfield, NJ, United States
Goldenberg, David M., Mendham, NJ, United States
PATENT ASSIGNEE(S): Center for Molecular Medicine and Immunology, Belleville, NJ, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5843894	19981201
APPLICATION INFO.:	US 1995-407899	19950321 (8)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Huff, Sheela
ASSISTANT EXAMINER: Reeves, Julie E.
LEGAL REPRESENTATIVE: Foley & Lardner
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Figure(s); 7 Drawing Page(s)
LINE COUNT: 825
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB **Kidney uptake** of antibody fragment conjugates in patients is reduced by **administration** to the patient of one or more compounds selected from the group consisting of **D-lysine**, poly-**D-lysine**, or poly-**L-lysine**, or pharmaceutically acceptable salts or carboxyl derivatives thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/012.000
INCLS: 530/300.000; 530/350.000; 530/324.000
NCL NCLM: 514/012.000
NCLS: 530/300.000; 530/324.000; 530/350.000

L14 ANSWER 10 OF 28 USPATFULL
ACCESSION NUMBER: 97:42628 USPATFULL
TITLE: Two-step pretargeting methods using improved biotin-active agent conjugates
INVENTOR(S): Reno, John M., Brier, WA, United States
Theodore, Louis J., Lynnwood, WA, United States
Searcher : Shears 308-4994

	Gustavson, Linda M., Seattle, WA, United States
PATENT ASSIGNEE(S):	NeoRx Corporation, Seattle, WA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5630996	19970520
APPLICATION INFO.:	US 1993-122979	19930916 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1992-995381, filed on 23 Dec 1992, now abandoned And Ser. No. US 1992-995383, filed on 23 Dec 1992, now abandoned , each Ser. No. US - which is a continuation-in-part of Ser. No. US 1992-895588, filed on 9 Jun 1992, now patented, Pat. No. US 5283342

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Eisenschenk, Frank C.
LEGAL REPRESENTATIVE: Burns, Doane, Swecker & Mathis, L.L.P.
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 22 Drawing Figure(s); 22 Drawing Page(s)
LINE COUNT: 4768
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods, compounds, compositions and kits that relate to pretargeted delivery of diagnostic and therapeutic agents are disclosed. In particular, methods for radiometal labeling of biotin and for improved radiohalogenation of biotin, as well as related compounds, are described. Also, clearing agents, anti-ligand-targeting moiety conjugates, target cell retention enhancing moieties and additional methods are discussed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/001.490
INCLS: 424/001.530; 424/009.363; 548/303.700; 548/304.100; 548/520.000; 548/526.000; 514/387.000; 540/474.000; 530/391.500; 530/391.300; 530/391.100; 546/283.100; 546/278.700
NCL NCLM: 424/001.490
NCLS: 424/001.530; 424/009.363; 514/387.000; 530/391.100; 530/391.300; 530/391.500; 540/474.000; 546/278.700; 546/283.100; 548/303.700; 548/304.100; 548/520.000; 548/526.000

L14 ANSWER 11 OF 28 USPATFULL
ACCESSION NUMBER: 97:36156 USPATFULL
TITLE: Clearing agents useful in pretargeting methods
INVENTOR(S): Axworthy, Donald B., Brier, WA, United States
Reno, John M., Brier, WA, United States
PATENT ASSIGNEE(S): NeoRx Corporation, Seattle, WA, United States

(U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5624896	19970429
APPLICATION INFO.:	US 1995-462765	19950605 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1993-163184, filed on 7 Dec 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-995381, filed on 23 Dec 1992, now abandoned which is a continuation-in-part of Ser. No. US 1992-895588, filed on 9 Jun 1992, now patented, Pat. No. US 5283342
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Eisenschenk, Frank C.
LEGAL REPRESENTATIVE: Burns, Doane, Swecker & Mathis, L.L.P.
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 12 Drawing Figure(s); 12 Drawing Page(s)
LINE COUNT: 3943
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel clearing agents are provided which comprise biotin analog containing clearance-directing moieties. Preferably such clearance-directing moieties endogenously contain or a rederivatized to expose galactose and/or mannose residues.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/008.000
INCLS: 530/350.000; 530/386.000; 530/362.000; 530/363.000; 530/402.000; 530/410.000; 548/303.700
NCL NCLM: 514/008.000
NCLS: 530/350.000; 530/362.000; 530/363.000; 530/386.000; 530/402.000; 530/410.000; 548/303.700

L14 ANSWER 12 OF 28 USPATFULL
ACCESSION NUMBER: 97:27275 USPATFULL
TITLE: Hexose derivatized human serum albumin clearing agents
INVENTOR(S): Axworthy, Donald B., Brier, WA, United States
Reno, John M., Brier, WA, United States
PATENT ASSIGNEE(S): NeoRx Corporation, Seattle, WA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5616690	19970401
APPLICATION INFO.:	US 1993-133613	19931008 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1992-995383, filed on 23 Dec 1992, now abandoned which is a

continuation-in-part of Ser. No. US 1992-895588, filed on 9 Jun 1992, now patented, Pat. No. US 5283342

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Eisenschenk, Frank C.
LEGAL REPRESENTATIVE: Burns, Doane, Swecker & Mathis, L.L.P.
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 22 Drawing Figure(s); 22 Drawing Page(s)
LINE COUNT: 2945
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel clearing agents comprising hexose derivatized human serum albumin and ligand molecule(s) are provided. These clearing agents are useful in pretargeting methods to clear previously administered anti-ligand containing conjugates. Preferably, the hexose is mannose or galactose and the ligand and anti-ligand are respectively biotin and avidin or streptavidin.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 530/363.000
INCLS: 548/303.700; 530/402.000
NCL NCLM: 530/363.000
NCLS: 530/402.000; 548/303.700

L14 ANSWER 13 OF 28 USPATFULL
ACCESSION NUMBER: 97:18284 USPATFULL
TITLE: Biotinidase-resistant biotin-DOTA conjugates
INVENTOR(S): Axworthy, Donald B., Brier, WA, United States
Theodore, Louis J., Lynnwood, WA, United States
Gustavson, Linda M., Seattle, WA, United States
Reno, John M., Brier, WA, United States
PATENT ASSIGNEE(S): NeoRx Corporation, Seattle, WA, United States (U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 5608060	19970304	
	WO 9325240	19931223	
APPLICATION INFO.:	US 1995-351469	19950221	(8)
	WO 1993-US5406	19930607	
		19950221	PCT 371 date
		19950221	PCT 102(e) date

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1992-995383, filed on 23 Dec 1992, now abandoned And a continuation-in-part of Ser. No. US 1992-995381, filed on 23 Dec 1992, now abandoned , each Ser. No. US - which is a continuation-in-part of Ser. No. US 1992-895588, filed on 9 Jun 1992, now patented, Pat. No. US 5283342, issued on 1 Feb

1994
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Eisenschenk, Frank C.
LEGAL REPRESENTATIVE: Burns, Doane, Swecker & Mathis, L.L.P.
NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 22 Drawing Figure(s); 22 Drawing Page(s)
LINE COUNT: 4732
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Biotinidase-resistant biotin-DOTA conjugates, and methods of use thereof in diagnostic and therapeutic pretargeting methods are provided. These conjugates are useful in diagnosis and treatment of cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 540/474.000
INCLS: 548/304.100; 536/001.110; 536/017.400; 536/053.000; 424/009.363
NCL NCLM: 540/474.000
NCLS: 424/009.363; 536/001.110; 536/017.400; 536/053.000; 548/304.100

L14 ANSWER 14 OF 28 USPATFULL
ACCESSION NUMBER: 96:108662 USPATFULL
TITLE: Three-step pretargeting methods using improved biotin-active agent
INVENTOR(S): Theodore, Louis J., Lynnwood, WA, United States
Reno, John M., Brier, WA, United States
Gustavson, Linda M., Seattle, WA, United States
PATENT ASSIGNEE(S): Neorx Corporation, Seattle, WA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5578287	19961126
APPLICATION INFO.:	US 1993-156614	19931123 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1992-995383, filed on 23 Dec 1992, now abandoned which is a continuation-in-part of Ser. No. US 1992-895588, filed on 9 Jun 1992, now patented, Pat. No. US 5283342
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Eisenschenk, Frank C.
LEGAL REPRESENTATIVE: Burns, Doane, Swecker & Mathis, L.L.P.
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT: 2318
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods, compounds, compositions and kits that relate to pretargeted delivery of diagnostic and therapeutic agents are disclosed. In particular, three-step pretargeting methods are described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/001.490
INCLS: 424/009.363; 424/001.530; 548/303.700; 514/387.000; 540/474.000; 530/391.500; 530/391.300; 530/391.100
NCL NCLM: 424/001.490
NCLS: 424/001.530; 424/009.363; 514/387.000; 530/391.100; 530/391.300; 530/391.500; 540/474.000; 548/303.700

L14 ANSWER 15 OF 28 USPATFULL
ACCESSION NUMBER: 96:68105 USPATFULL
TITLE: Pretargeting methods and compounds
INVENTOR(S): Yau, Eric K., Kirkland, WA, United States
Theodore, Louis J., Lynnwood, WA, United States
Gustavson, Linda M., Seattle, WA, United States
PATENT ASSIGNEE(S): NeoRx Corporation, Seattle, WA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5541287	19960730
APPLICATION INFO.:	US 1994-345811	19941122 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1993-156565, filed on 22 Nov 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-995381, filed on 23 Dec 1992, now abandoned which is a continuation-in-part of Ser. No. US 1992-895588, filed on 9 Jun 1992, now patented, Pat. No. US 5283342, issued on 1 Feb 1994
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Chan, Christina Y.
ASSISTANT EXAMINER: Prickril, Benet
LEGAL REPRESENTATIVE: Burns, Doane, Swecker & Mathis, L.L.P.
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 17 Drawing Figure(s); 17 Drawing Page(s)
LINE COUNT: 4365
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods, compounds, compositions and kits that relate to pretargeted delivery of diagnostic and therapeutic agents are disclosed. In particular, methods for radiometal labeling of biotin, as well as related compounds, are described. Articles of manufacture useful in pretargeting methods are also discussed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
Searcher : Shears 308-4994

INCL INCLM: 530/317.000
INCLS: 530/330.000; 530/331.000; 530/332.000; 530/323.000; 530/345.000
NCL NCLM: 530/317.000
NCLS: 530/323.000; 530/330.000; 530/331.000; 530/332.000; 530/345.000

L14 ANSWER 16 OF 28 USPATFULL

ACCESSION NUMBER:	94:53279 USPATFULL
TITLE:	Alteration of pharmacokinetics of proteins by charge modification
INVENTOR(S):	Morgan, Jr., Alton C., Edmonds, WA, United States Sivam, Gowsala P., Edmonds, WA, United States Abrams, Paul G., Seattle, WA, United States
PATENT ASSIGNEE(S):	NeoRx Corporation, Seattle, WA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5322678	19940621
APPLICATION INFO.:	US 1988-157273	19880217 (7)

DOCUMENT TYPE:	Utility
PRIMARY EXAMINER:	Lovering, Richard D.
ASSISTANT EXAMINER:	Covert, John M.
LEGAL REPRESENTATIVE:	Picard, Roberta A.
NUMBER OF CLAIMS:	11
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	8 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT:	792

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB There is disclosed charge-modified conjugates comprising a targeting protein bound to a therapeutic or diagnostic agent. Charge-modifying a conjugate to cause an acidic shift in the isoelectric point results in prolonged serum half-life upon in vivo administration and is useful to accumulate a therapeutic agent at the target site. Conversely, charge-modification to cause a basic shift in the isoelectric point of the conjugate reduces serum half-life upon in vivo use for diagnostic imaging purposes and results in higher target-to-background ratios.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/001.530
INCLS: 424/001.490; 424/085.910; 530/391.300; 530/391.500; 530/391.700; 530/402.000; 530/410.000
NCL NCLM: 424/001.530
NCLS: 424/001.490; 424/178.100; 424/182.100; 530/391.300; 530/391.500; 530/391.700; 530/402.000; 530/410.000

L14 ANSWER 17 OF 28 USPATFULL

ACCESSION NUMBER: 94:17779 USPATFULL
TITLE: Nephro protective infusion solutions
INVENTOR(S): Bertermann, Hagen, Flensburger Strasse 83, D-2300 Kiel, Germany, Federal Republic of

	NUMBER	DATE
PATENT INFORMATION:	US 5290538	19940301
APPLICATION INFO.:	US 1992-873579	19920421 (7)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1990-566365, filed on 15 Oct 1990, now abandoned	
PRIORITY INFORMATION:	DE 1988-3843241	19881222

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Waddell, Frederick E.
ASSISTANT EXAMINER: Hook, Gregory
LEGAL REPRESENTATIVE: Larson, Herbert W.
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
LINE COUNT: 325
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention herein is a method of protecting against renal damage in a patient receiving carboplatin, cyclosporine A or cisplatin comprising administering to said patient the following mixture of amino acids consisting of glycine, L-alanine, L-serine, L-threonine, L-valine, L-leucine, L-isoleucine and L-proline.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/010.000
INCLS: 514/423.000; 514/561.000; 514/922.000
NCL NCLM: 514/561.000
NCLS: 514/423.000; 514/922.000

L14 ANSWER 18 OF 28 USPATFULL
ACCESSION NUMBER: 94:9678 USPATFULL
TITLE: Biotinylated small molecules
INVENTOR(S): Gustavson, Linda M., Seattle, WA, United States
Srinivasan, Ananthachari, St. Charles, MO, United States
Fritzberg, Alan R., Edmonds, WA, United States
Reno, John M., Brier, WA, United States
Axworthy, Donald B., Brier, WA, United States
PATENT ASSIGNEE(S): NeoRx Corporation, Seattle, WA, United States (U.S. corporation)

	NUMBER	DATE

Searcher : Shears 308-4994

PATENT INFORMATION: US 5283342 19940201
APPLICATION INFO.: US 1992-895588 19920609 (7)
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Higel, Floyd D.
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1,3
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT: 911
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods, compounds, compositions and kits that relate to pretargeted delivery of diagnostic and therapeutic agents are disclosed. In particular, methods for radiometal labeling of biotin and for improved radiohalogenation of biotin, as well as related compounds, are described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 548/304.100
INCLS: 435/005.000; 435/006.000; 435/009.000; 436/804.000; 436/808.000; 436/544.000; 436/545.000; 534/014.000; 534/015.000
NCL NCLM: 548/304.100
NCLS: 435/005.000; 435/006.000; 436/544.000; 436/545.000; 436/804.000; 436/808.000; 534/014.000; 534/015.000

L14 ANSWER 19 OF 28 USPATFULL
ACCESSION NUMBER: 93:74285 USPATFULL
TITLE: Renin inhibitors
INVENTOR(S): Bender, Wolfgang, Wuppertal, Germany, Federal Republic of
Kinast, Gunther, Wuppertal, Germany, Federal Republic of
Knorr, Andreas, Erkrath, Germany, Federal Republic of
Stasch, Johannes-Peter, Wuppertal, Germany, Federal Republic of
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Leverkusen, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5242903	19930907
APPLICATION INFO.:	US 1991-771077	19911002 (7)
RELATED APPLN. INFO.:	Division of Ser. No. US 1990-553493, filed on 13 Jul 1990, now patented, Pat. No. US 5095006	
PRIORITY INFORMATION:	DE 1989-3926021	19890805
	DE 1990-4004820	19900216

Searcher : Shears 308-4994

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Griffin, Ronald W.
LEGAL REPRESENTATIVE: Sprung Horn Kramer & Woods
NUMBER OF CLAIMS: 1
EXEMPLARY CLAIM: 1
LINE COUNT: 2680
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Renin-inhibiting peptides of the formula ##STR1## in which X represents a group of the formula ##STR2## represents hydroxyl, alkoxy having up to 8 carbon atoms, benzyloxy or a group of the formula --NR.sup.4 R.sup.5,

A, B, D and E are identical or different and in each case

represent a direct bond,

represent a radical of the formula ##STR3## in which Z denotes oxygen, sulphur or the methylene group

represents a grouping of the formula ##STR4## m represents a number 0, 1 or 2, and L represents a group of the formula --CH.sub.2 --NR2R.sub.3

and physiologically acceptable salts thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/018.000
INCLS: 514/019.000; 530/323.000; 530/330.000; 530/331.000; 548/314.700; 548/338.100; 548/312.100; 548/315.100; 548/312.400; 562/445.000
NCL NCLM: 514/018.000
NCLS: 514/019.000; 530/323.000; 530/330.000; 530/331.000; 548/312.100; 548/312.400; 548/314.700; 548/315.100; 548/338.100; 562/445.000

L14 ANSWER 20 OF 28 USPATFULL
ACCESSION NUMBER: 92:84972 USPATFULL
TITLE: Polychelating agents for image and spectral enhancement (and spectral shift)
INVENTOR(S): Ranney, David F., Dallas, TX, United States
PATENT ASSIGNEE(S): Access Pharmaceuticals Inc., Dallas, TX, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5155215	19921013
APPLICATION INFO.:	US 1990-613465	19901107 (7)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1985-799757, filed on 18 Nov 1985, now abandoned
Searcher : Shears 308-4994

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Maples, John S.
LEGAL REPRESENTATIVE: Arnold, White & Durkee
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
LINE COUNT: 1589
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention includes an image-enhancing agent comprising a biodegradable, water-soluble polymer, synthetic or naturally derived and having repeating hydrophilic monomeric units with amino or hydroxyl groups. This agent also includes chelating agents comprising functional groups bound to an amino or bydroxyl group of the monomeric units. These chelating agents have a formation constant for divalent or trivalent metal cations of at least about 10.sup.8 at physiological temperature and pH. This image-enhancing agent is biodegradable to intermediary metabolites, excretable chelates, oligomers, monomers or combinations thereof of low toxicity.

These image-enhancing agents may further comprise a paramagnetic metal ion for enhancement of the image arising from induced magnetic resonance signals.

Images resulting from scanning of gamma particle emissions may be enhanced when the image-enhancing agent of the present invention comprise radioisotopic metal ions emitting gamma particles.

The physical conversion of these image enhancing agents into microspheres allows further internal directioning of the image-enhancing agents to organs with phogocytic capabilities.

Dextran is a preferred polymer DTPA and gadoliniium are respectively preferred chelating agents and paramagnetic metal ions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 534/016.000
INCLS: 536/017.100; 536/021.000; 536/051.000; 536/112.000; 536/113.000; 536/121.000
NCL NCLM: 534/016.000
NCLS: 536/017.100; 536/021.000; 536/051.000; 536/112.000; 536/113.000; 536/121.000

L14 ANSWER 21 OF 28 USPATFULL
ACCESSION NUMBER: 92:61899 USPATFULL
TITLE: Nutrient composition
INVENTOR(S): Hara, Takahiro, Machida, Japan
Furukawa, Tadayasu, Chesterfield, MO, United States
Searcher : Shears 308-4994

PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Tokyo, Japan
(non-U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 5134125	19920728	
	WO 9011024	19901004	
APPLICATION INFO.:	US 1990-613687	19901019	(7)
	WO 1990-JP651	19900522	
		19901019	PCT 371 date
		19901019	PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1989-75778	19890328

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Schain, Howard E.
ASSISTANT EXAMINER: Koh, Choon P.
LEGAL REPRESENTATIVE: Antonelli, Terry, Stout & Kraus
NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 317
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to nutrient compositions for mammals comprising L-glutamyl-L-glutamine.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/019.000
INCLS: 426/656.000
NCL NCLM: 514/019.000
NCLS: 426/656.000

L14 ANSWER 22 OF 28 USPATFULL
ACCESSION NUMBER: 92:27516 USPATFULL
TITLE: Nutrient composition
INVENTOR(S): Furukawa, Tadayasu, Chesterfield, MO, United States
Hara, Takahiro, Machida, Japan
PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Tokyo, Japan
(non-U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 5102871	19920407	
APPLICATION INFO.:	US 1990-510876	19900418	(7)

	NUMBER	DATE

PRIORITY INFORMATION: JP 1989-104261 19890424
JP 1989-334483 19891222
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Lee, Lester L.
ASSISTANT EXAMINER: Marshall, S. G.
LEGAL REPRESENTATIVE: Antonelli, Terry Stout & Kraus
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT: 449
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Nutrient compositions useful as amino acid infusions comprise L-glutamyl-L-cystine and/or L-glutamyl-L-cysteine disulfide. The nutrient compositions can achieve extremely high utilization of cysteine and cystine which could not be hitherto used as nutrient compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/011.000
INCLS: 530/331.000
NCL NCLM: 514/019.000
NCLS: 514/018.000; 530/331.000

L14 ANSWER 23 OF 28 USPATFULL
ACCESSION NUMBER: 92:18951 USPATFULL
TITLE: Renin inhibitors having all retro-inverted peptide bonds
INVENTOR(S): Bender, Wolfgang, Wuppertal, Germany, Federal Republic of
Kinast, Gunther, Wuppertal, Germany, Federal Republic of
Knorr, Andreas, Erkrath, Germany, Federal Republic of
Stasch, Johannes-Peter, Wuppertal, Germany, Federal Republic of
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Leverkusen, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 5095006	19920310	
APPLICATION INFO.:	US 1990-553493	19900713	(7)

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1989-3926021	19890508
	DE 1990-4004820	19900216

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Wax, Robert A.
Searcher : Shears 308-4994

ASSISTANT EXAMINER: Walsh, Stephen
LEGAL REPRESENTATIVE: Sprung Horn Kramer & Woods
NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
LINE COUNT: 2702
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Renin-inhibiting peptides of the formula ##STR1## in which X represents a group of the formula ##STR2## represents hydroxyl, alkoxy having up to 8 carbon atoms, benzyloxy or a group of the formula --NR.sup.4 R.sup.5,

A, B, D and E are identical or different and in each case

represent a direct bond,

represent a radical of the formula ##STR3## in which Q1 denotes oxygen, sulphur or the methylene group

represent a grouping of the formula ##STR4## m represents a number 0, 1 or 2, and L represents a group of the formula --CH.sub.2 NR.sup.2 R.sup.3

and physiologically acceptable salts thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/019.000
INCLS: 514/018.000; 530/323.000; 530/331.000; 530/332.000; 548/344.000; 562/445.000
NCL NCLM: 514/019.000
NCLS: 514/018.000; 530/323.000; 530/331.000; 530/332.000; 548/338.100; 562/445.000

L14 ANSWER 24 OF 28 USPATFULL
ACCESSION NUMBER: 92:7449 USPATFULL
TITLE: Immunoconjugates and methods for their use in tumor therapy
INVENTOR(S): Hellstrom, Karl E., Seattle, WA, United States
Hellestrom, Ingegerd E., Seattle, WA, United States
Lavie, Efraim, Seattle, WA, United States
PATENT ASSIGNEE(S): Oncogen, Seattle, WA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5084560	19920128
APPLICATION INFO.:	US 1990-564387	19900807 (7)

RELATED APPLN. INFO.: Division of Ser. No. US 1987-47161, filed on 12 May 1987, now patented, Pat. No. US 4997913 which
Searcher : Shears 308-4994

is a continuation-in-part of Ser. No. US 1986-880674, filed on 30 Jun 1986, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Russel, Jeffrey E.
ASSISTANT EXAMINER: Kim, Kay
LEGAL REPRESENTATIVE: Mandel, SaraLynn
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 15 Drawing Figure(s); 15 Drawing Page(s)
LINE COUNT: 822
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel pH-sensitive immunoconjugates which dissociate in low-pH tumor tissue, comprising a chemotherapeutic agent and an antibody reactive with a tumor-associated antigen are described. The chemotherapeutic agent is coupled to the antibody by a link which is unstable in low pH. The link may comprise a spacer consisting of a polyamino acid. Representative antibodies for use in these immunoconjugates include monoclonal antibodies which are not internalized by tumor cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 530/390.000
INCLS: 530/391.000; 424/085.910
NCL NCLM: 530/391.900
NCLS: 424/181.100; 530/388.800; 530/388.850

L14 ANSWER 25 OF 28 USPATFULL
ACCESSION NUMBER: 91:19030 USPATFULL
TITLE: pH-sensitive immunoconjugates and methods for their use in tumor therapy
INVENTOR(S): Hellstrom, Karl E., Seattle, WA, United States
Hellstrom, Ingegerd E., Seattle, WA, United States
Lavie, Efraim, Seattle, WA, United States
PATENT ASSIGNEE(S): Oncogen, Seattle, WA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 4997913	19910305
APPLICATION INFO.:	US 1987-47161	19870512 (7)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1986-880674, filed on 30 Jun 1986, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Draper, Garnette D.
LEGAL REPRESENTATIVE: Mandel, SaraLynn
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 15 Drawing Figure(s); 15 Drawing Page(s)
Searcher : Shears 308-4994

LINE COUNT: 952
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel pH-sensitive immunoconjugates which dissociate in low-pH tumor tissue, comprising a chemotherapeutic agent and an antibody reactive with a tumor-associated antigen are described. The chemotherapeutic agent is coupled to the antibody by a link which is unstable in low pH. The link may comprise a spacer consisting of a polyamino acid. Representative antibodies for use in these immunoconjugates include monoclonal antibodies which are not internalized by tumor cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 530/389.000
INCLS: 530/390.000; 530/391.000; 530/810.000; 530/812.000; 424/085.910; 424/009.000; 514/002.000; 514/008.000; 514/021.000; 514/885.000
NCL NCLM: 424/181.100
NCLS: 514/002.000; 514/008.000; 514/021.000; 514/885.000; 530/388.850; 530/391.900; 530/810.000; 530/812.000

L14 ANSWER 26 OF 28 USPATFULL
ACCESSION NUMBER: 89:25837 USPATFULL
TITLE: Renin inhibitors and aminoacid and aminoaldehyde derivatives
INVENTOR(S): Bender, Wolfgang, Wuppertal, Germany, Federal Republic of
Henning, Rolf, Wuppertal, Germany, Federal Republic of
Knorr, Andreas, Erkrath, Germany, Federal Republic of
Stasch, Johannes-Peter, Wuppertal, Germany, Federal Republic of
PATENT ASSIGNEE(S): Bayer Aktiengesellschaft, Leverkusen, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 4818748	19890404	
APPLICATION INFO.:	US 1987-22710	19870306	(7)

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1986-3608209	19860312
	DE 1986-3628650	19860823

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Phillips, Delbert R.
LEGAL REPRESENTATIVE: Sprung Horn Kramer & Woods
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
Searcher : Shears 308-4994

LINE COUNT: 2811
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Anti-hypertensive compounds of the formula ##STR1## in which A represents hydrogen, C.sub.1 -C.sub.8 -alkyl, C.sub.7 -C.sub.14 -aralkyl, phenylsulphonyl, tolylsulphonyl or C.sub.1 -C.sub.8 -alkylsulfphonyl, or represents an aminoprotective group,

B represents a direct bond, or represents sarcosyl, or represents a group of the formula ##STR2## D represents a direct bond, or represents a group of the formula ##STR3## wherein X represents methylene, ethylene or sulphur,

E, G, J, K, L and M independently have the same meanings as B,

R.sup.1 is an optionally substituted phenyl radical, and

Q is a hydroxy, alkoxy or amino group, or a physiologically acceptable salt thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/016.000
INCLS: 514/017.000; 514/018.000; 514/019.000; 530/328.000; 530/329.000; 530/330.000; 530/331.000
NCL NCLM: 514/016.000
NCLS: 514/017.000; 514/018.000; 514/019.000; 530/328.000; 530/329.000; 530/330.000; 530/331.000; 530/860.000; 930/020.000; 930/021.000; 930/030.000; 930/250.000

L14 ANSWER 27 OF 28 USPATFULL
ACCESSION NUMBER: 81:2484 USPATFULL
TITLE: Human serum plasminogen activator
INVENTOR(S): Reich, Edward, New York, NY, United States
Guha, Arabinda, Pelham Manor, NY, United States
Schleuning, Wolf-Dieter, New York, NY, United States
PATENT ASSIGNEE(S): Rockefeller University, New York, NY, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 4245051	19810113
APPLICATION INFO.:	US 1978-891808	19780330 (5)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Shapiro, Lionel M.
LEGAL REPRESENTATIVE: Haight, Rosfeld, Noble & Santa Maria
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
LINE COUNT: 804
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A plasminogen proactivator and a corresponding activator has been isolated from mammalian and avian, especially human, plasma which is characterized within a given species as a single, electrophoretically and immunologically homogeneous protein. The activator acts as a catalyst to initiate fibrinolytic activity in plasma and is therefore useful in controlling clotting which occurs, e.g. in venous thrombosis or arterial occulsion, and in diagnosing conditions which predispose to thromboembolic phenomena. The proactivator has a long useful in vivo half life and can be used to provide a reservoir for maintaining the fibrolytic potential of blood.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/212.000
INCLS: 260/112.000B; 424/101.000
NCL NCLM: 435/212.000
NCLS: 424/531.000; 530/395.000; 530/830.000; 530/831.000

L14 ANSWER 28 OF 28 USPATFULL

ACCESSION NUMBER:	78:36356 USPATFULL
TITLE:	Therapeutic compositions comprising alpha-hydroxy analogs of essential amino acids and their administration to humans for promotion of protein synthesis and suppression of urea formation
INVENTOR(S):	Walser, Mackenzie, Ruxton, MD, United States
PATENT ASSIGNEE(S):	The Johns Hopkins University, Baltimore, MD, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 4100160	19780711
APPLICATION INFO.:	US 1976-669588	19760323 (5)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1974-461259, filed on 15 Apr 1974, now abandoned And Ser. No. US 1974-461260, filed on 15 Apr 1974, now abandoned , each which is a continuation-in-part of Ser. No. US 1973-355326, filed on 30 Apr 1973, now abandoned And Ser. No. US 1973-355327, filed on 30 Apr 1973, now abandoned , said Ser. No. 355327 which is a continuation-in-part of Ser. No. US 1972-270986, filed on 12 Jul 1972, now abandoned

DOCUMENT TYPE:	Utility
PRIMARY EXAMINER:	Schenkman, Leonard
LEGAL REPRESENTATIVE:	Seidel, Gonda & Goldhammer
NUMBER OF CLAIMS:	30
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	1 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT:	1284

Searcher : Shears 308-4994

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compositions containing the hydroxy analogs of certain essential amino acids are formulated for therapeutic use, particularly in the treatment of renal disorders, hepatic failure and conditions of protein wasting in human subjects. In preferred embodiments, keto analogs of certain essential amino acids are used in combination with hydroxy analogs of other essential amino acids.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 424/274.000
INCLS: 424/317.000; 424/319.000
NCL NCLM: 514/400.000
NCLS: 514/419.000; 514/557.000; 514/561.000; 514/564.000; 514/565.000; 514/570.000; 514/893.000

FILE 'REGISTRY' ENTERED AT 10:17:59 ON 09 MAY 2000
E ONCONASE/CN 5
L15 1 SEA ABB=ON PLU=ON ONCONASE/CN
E RIBONUCLEASE/CN 5
E RIBONUCLEASE/CN
L16 215 SEA ABB=ON PLU=ON RIBONUCLEASE ?/CN
L17 216 SEA ABB=ON PLU=ON L15 OR L16

FILE 'CAPLUS' ENTERED AT 10:18:53 ON 09 MAY 2000
L18 31825 SEA ABB=ON PLU=ON L17 OR RIBONUCLEASE OR ONCONASE OR (RIBONUCLEIC OR RIBO NUCLEIC)(1W)BIND?(W)PROTEIN
L19 242 SEA ABB=ON PLU=ON L18 AND (L3 OR (D OR L)(W)(LYSINE OR LYS))
L20 8 SEA ABB=ON PLU=ON L19 AND (KIDNEY OR RENAL?)
L21 8 SEA ABB=ON PLU=ON L20 NOT L9

L21 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:260484 CAPLUS
TITLE: Methods for identifying inhibitors of post-Amadori advanced glycation endproduct (AGE) formation, inhibiting oxidative modification of proteins, and treating lipid peroxidation and atherosclerosis
INVENTOR(S): Baynes, John; Onorato, Joelle; Thorpe, Suzanne; Khalifah, Raja; Hudson, Billy
PATENT ASSIGNEE(S): Kansas University Medical Center, USA; University of South Carolina
SOURCE: PCT Int. Appl., 156 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000022094	A2	20000420	WO 1999-US23702	19991008

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-PV103795 19981009

AB Compns. and methods are provided for modeling post-Amadori AGE formation and the identification and characterization of effective inhibitors of post-Amadori AGE formation, and such identified inhibitor compns. Also provided are methods to treat or prevent oxidative modification of proteins, including LDL, to treat or prevent lipid peroxidn., and to treat or prevent atherosclerosis, comprising administering an amt. effective of one of the compds. of the invention to treat or prevent the disorder. Inhibitors of the invention include benzene and pyridine derivs, e.g. pyridoxamine.

IT INDEXING IN PROGRESS

IT **9001-99-4**

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(A; methods for identifying inhibitors of post-Amadori AGE formation, inhibiting oxidative modification of proteins, and treating lipid peroxidn. and atherosclerosis)

L21 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1997:555607 CAPLUS

DOCUMENT NUMBER: 127:245075

TITLE: Standardizing the immunological measurement of advanced glycation end products using normal human serum

AUTHOR(S): Mitsuhashi, Tomoko; Vlassara, Helen; Founds, H. W.; Li, Yong Ming

CORPORATE SOURCE: The Picower Institute for Medical Research, 350 Community Drive, Manhasset, NY, 11030, USA

SOURCE: J. Immunol. Methods (1997), 207(1), 79-88
CODEN: JIMMBG; ISSN: 0022-1759

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Advanced glycation end products (AGEs) have been linked to many sequelae of diabetes, **renal** disease, and aging. To detect AGE levels in human tissues and blood samples, a competitive ELISA has been widely used. As no consensus or std. research method for

the quantitation of AGEs currently exists, nor is a universally defined AGE unit available, the comparative quantitation of AGEs between research labs. is problematic and restricts the usefulness of interlab. clin. data. By comparing the cross-reactivities of 5 different anti-AGE antisera with 5 different in vitro AGE-modified proteins, we found that the immunol. recognition of AGEs by competitive ELISA is both AGE-carrier protein- and anti-AGE antibody-dependent. This suggests that in vitro AGE-modified proteins might not be appropriate stds. for AGEs that occur naturally in vivo. Based on our observation that serum AGE levels in the normal human population are consistently within a narrow range and several-fold lower than in diabetics, we propose a method to standardize AGE units against normal human serum (NHS). In this new method, one AGE unit is defined as the inhibition that results from 1:5 dild. NHS in the competitive AGE-ELISA; thus the AGE value in NHS is 5 units/mL. This NHS method requires a competitive AGE-ELISA with reasonable sensitivity such that 1:5 NHS produces a 25-40% inhibition of anti-AGE antibody binding to immobilized AGE-proteins. By using this standardized method we found that the AGE levels in normal human serum (5.0 .+-. 2.2 units/mL) fit a normal distribution (.chi.2-test), and the serum AGE levels in diabetic patients (20.3 .+-. 3.8 units/mL) are significantly higher than that of the normal population. Since AGE units can now be defined against a universally available std., NHS, the results of quant. AGE measurements using this method should be comparable between assays and between different labs. Taken together, standardizing the AGE-ELISA protocol as described here provides a simple and quant. method that should facilitate the expanded application of clin. AGE data.

IT **9001-99-4D**, **RNase**, AGE-modified
25104-18-1D, Poly-**L-lysine**, AGE-modified
38000-06-5D, Poly-**L-lysine**, AGE-modified
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(ELISA stds. for advanced glycation end products using normal human serum)

L21 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:335556 CAPLUS
DOCUMENT NUMBER: 126:327767
TITLE: Immunochemical detection of in vivo advanced glycosylation end products [AGE]
INVENTOR(S): Bucala, Richard J.
PATENT ASSIGNEE(S): Rockefeller University, USA
SOURCE: U.S., 29 pp. Cont.-in-part of U.S. Ser. No. 811,579, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5624804	A	19970429	US 1992-956849	19921001
CN 1079825	A	19931222	CN 1992-115235	19921219
WO 9313421	A1	19930708	WO 1992-US11158	19921221
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9334187	A1	19930728	AU 1993-34187	19921221
AU 681340	B2	19970828		
EP 623216	A1	19941109	EP 1993-902713	19921221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07502534	T2	19950316	JP 1992-511864	19921221
US 5629408	A	19970513	US 1995-476381	19950607
US 5683887	A	19971104	US 1995-487055	19950607
US 5702704	A	19971230	US 1995-486513	19950607
US 5712101	A	19980127	US 1995-472398	19950607
US 5733546	A	19980331	US 1995-484869	19950607
PRIORITY APPLN. INFO.:			US 1991-811579	19911220
			US 1992-956849	19921001
			WO 1992-US11158	19921221

AB The circulating advanced glycosylation end products Hb-AGE, serum AGE-peptides, and urinary AGE-peptides are disclosed as long-term markers of diseases and dysfunctions having as a characteristic the presence of a measurable difference in AGE concn. Diagnostic and therapeutic protocols taking advantage of the characteristics of these AGEs are disclosed. Antibodies which recognize and bind to in vivo-derived AGEs are also disclosed. Methods of using these antibodies as well as pharmaceutical compns. are also disclosed, along with numerous diagnostic applications, including methods for the measurement of the presence and amt. of AGEs in both plants and animals, including humans, as well as in cultivated and synthesized protein material for therapeutic use.

IT **9001-99-4D**, **RNase**, AGE-contg.
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(advanced glycosylation end products immunoassay in vivo in disease diagnosis)

L21 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1993:535029 CAPLUS
DOCUMENT NUMBER: 119:135029
TITLE: Immunochemical detection of in vivo advanced glycosylation endproducts (AGEs)
INVENTOR(S): Bucala, Richard J.

PATENT ASSIGNEE(S): Rockefeller University, USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9313421	A1	19930708	WO 1992-US11158	19921221
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
US 5624804	A	19970429	US 1992-956849	19921001
AU 9334187	A1	19930728	AU 1993-34187	19921221
AU 681340	B2	19970828		
EP 623216	A1	19941109	EP 1993-902713	19921221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07502534	T2	19950316	JP 1992-511864	19921221
PRIORITY APPLN. INFO.:			US 1991-811579	19911220
			US 1992-956849	19921001
			WO 1992-US11158	19921221

AB Circulating Hb-AGE, serum AGE-peptides, and urinary AGE-peptides are disclosed as long-term markers of diseases and dysfunctions having as a characteristic the presence of a measurable difference in AGE concn. Diagnostic and therapeutic protocols taking advantage of the characteristics of these AGEs are disclosed. Antibodies which recognize and bind to in vivo-derived AGEs are also disclosed, as are methods using the antibodies, pharmaceutical compns., diagnostic applications, etc. Prepn. of polyclonal anti-AGE antibodies, AGE formation kinetics, diabetes evaluation, etc. are described.

IT **25104-18-1**, Poly-**L-lysine**
38000-06-5, Poly-**L-lysine**, SRU
RL: ANST (Analytical study)
(advanced glycosylation endproducts immunochem. detection in analyte sample of)

IT **9001-99-4D**, advanced glycosylation endproducts
RL: ANST (Analytical study)
(antiserum to)

L21 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1991:3990 CAPLUS
DOCUMENT NUMBER: 114:3990
TITLE: Membrane destruction by polyamines
AUTHOR(S): Fukushima, Yoshihiro
CORPORATE SOURCE: Natl. Child. Med. Res. Cent., Tokyo, 154, Japan

SOURCE: Biomed. Res. (1990), 11(5), 345-52
CODEN: BRESD5; ISSN: 0388-6107
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Treatment of membranes from the sheep **kidney** or rat brain with polyamines (spermidine, histone, or polylysine) at 0.degree. disrupted the membrane structure. The recovery of membrane proteins and phospholipids was decreased in the ppt. and increased in the supernatant of the treated membranes after centrifugation. The polyamines converted the membranes to buoyant particles. As various naturally occurring low-mol.-wt. polyamines and synthetic or natural polypeptides generally destabilized the membrane, it appeared that no specific polyamine conformation was required; the pos. charged amino groups alone seemed to be sufficient. High concns. of monovalent salts such as ammonium sulfate or lithium chloride stabilized the membranes against the polyamines. In the presence of a low concn. of SDS (at which SDS itself had no effect on membrane stability), even monoamines such as arginine disrupted the membrane at high concns.

IT **9001-99-4, Ribonuclease 25104-18-1,** Poly-**L-lysine 38000-06-5,** Poly-**L-lysine**
RL: BIOL (Biological study)
(cell membrane degrdn. by, salts interaction with)

L21 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1982:67142 CAPLUS
DOCUMENT NUMBER: 96:67142
TITLE: Role of leukocyte factors and cationic polyelectrolytes in phagocytosis of group A streptococci and Candida albicans by neutrophils, macrophages, fibroblasts and epithelial cells: modulation by anionic polyelectrolytes in relation to pathogenesis of chronic inflammation
AUTHOR(S): Ginsburg, Isaac; Sela, Michael N.; Morag, Abraham; Ravid, Zohar; Duchan, Zvia; Ferne, Mina; Rabinowitz-Bergner, Sonia; Thomas, Peter Page; Davies, Philip; et al.
CORPORATE SOURCE: Hadassah Sch. Dent. Med., Hebrew Univ., Jerusalem, Israel
SOURCE: Inflammation (N. Y.) (1981), 5(4), 289-312
CODEN: INFLD4; ISSN: 0360-3997
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A variety of cationic polyelectrolytes opsonized group A streptococci and C. albicans to phagocytosis by human polymorphonuclear leukocytes and by mouse peritoneal macrophages. The most potent opsonins for streptococci were specific antibodies

supplemented with complement, nuclear histone, polylysine, polyarginine, **RNase**, leukocyte lysates, leukocyte cationic protein and, to a lesser extent, lysozyme and myeloperoxidase. Histone, **RNase**, leukocyte exts., and platelet exts. also functioned as opsonins for phagocytosis of streptococci in the peritoneal cavity, where phagocytic indexes, higher than those obtained for the in vitro phagocytosis, were obtained. Fresh serum, polylysine, polyarginine, and nuclear histone acted as good opsonins for Candida, but none of the other factors tested were active. In order for the cationic proteins and leukocyte exts. to function as opsonins, they must be present on the particle surface. These agents were poor opsonins when applied on the macrophages. Nuclear histone, polylysine, polyarginine, and fresh human serum also functioned as good opsonins for the uptake of Candida by mouse fibroblasts. On the other hand, none of the other substances which opsonized streptococci were effective with Candida. The phagocytic capabilities of fibroblast polykaryons were much higher than those of ordinary spindle-shaped mouse fibroblasts. Histone also functioned as a good opsonic agent for the uptake of Candida by human fibroblasts, HeLa cells, epithelial cells, monkey **kidney** cells, and rat heart cells. On the other hand, neither leukocyte exts. nor **RNase** LCP or MPO functioned as opsonins for these mammalian cells. Candida, Taken up by fibroblasts, were present within tight phagosomes, but no fusion of lysosomes with the phagosome occurred. A small proportion of the internalized yeast cells underwent partial plasmolysis, but little damage to the rigid cell walls was obsd. within 24-48 h of internalization. Phagocytosis of streptococci and Candida by macrophages and the uptake of Candida by fibroblasts were both strongly inhibited by liquoid (polyanethole sulfonic acid sodium salt). This anionic polyelectrolyte also markedly inhibited the release of N-acetylglucosaminidase from macrophages without affecting cell viability. Hyaluronic acid, DNA, and dextran sulfate markedly inhibited the uptake of histone-coated particles by macrophages. On the other hand, hyaluronic acid and DNA enhanced the uptake of Candida by fibroblasts. The effect of these anionic polyelectrolytes on phagocytosis of serum-opsonized particles by macrophages was not consistent. While in some expts. it blocked phagocytosis, in others it either had no effect or even enhanced the uptake of the particles. Phagocytosis of microorganisms by nonprofessional phagocytes like fibroblasts and the paucity in these cells of hydrolases capable of breaking down microbial cell wall components may contribute to the persistence of nonbiodegradable components of bacteria in tissues and to the perpetuation of chronic inflammatory sequellae. Cationic polyelectrolytes may also prove important as helper opsonins and as agents capable of enhancing the penetration into cells of both viable and nonviable particles, genetic material, and drugs.

IT **9001-99-4 25104-18-1 38000-06-5**

RL: BIOL (Biological study)
(as opsonins, in phagocytosis of Streptococcus and Candida, inflammation in relation to)

L21 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1981:474555 CAPLUS
DOCUMENT NUMBER: 95:74555
TITLE: Inhibition of **renal** accumulation of lysozyme (basic low molecular weight protein) by basic proteins and other basic substances
AUTHOR(S): Cojocel, C.; Franzen-Sieveking, M.; Beckmann, G.; Baumann, K.
CORPORATE SOURCE: Physiol. Inst., Univ. Hamburg, Hamburg, D-2000/13, Fed. Rep. Ger.
SOURCE: Pfluegers Arch. (1981), 390(3), 211-15
CODEN: PFLABK; ISSN: 0031-6768
DOCUMENT TYPE: Journal
LANGUAGE: English
AB When rats were given egg white lysozyme [9001-63-2] (7 nmol, i.v.), 31.7% of the injected dose was accumulated in the **kidneys**. Basic substances, such as cytochrome c [9007-43-6], **RNase** [**9001-99-4**], spermine tetrahydrochloride [306-67-2], L-arginine [74-79-3], and **L-lysine** [56-87-1], inhibited lysozyme accumulation, whereas the neutral myoglobulin had no effect. Proximal tubular lysozyme reabsorption was inhibited by cytochrome c in a dose-dependent fashion.
IT **9001-99-4**
RL: PRP (Properties)
(lysozyme accumulation by **kidney** inhibition by)

L21 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1973:451652 CAPLUS
DOCUMENT NUMBER: 79:51652
TITLE: Poly(riboinosinic acid) more important than poly(ribocytidylic acid) in the interferon induction process by poly(riboinosinic acid).poly(ribocytidylic acid)
AUTHOR(S): De Clercq, Erik; Stewart, William E., II; De Somer, Pierre
CORPORATE SOURCE: Rega Inst. Med. Res., Univ. Leuven, Louvain, Belg.
SOURCE: Virology (1973), 54(1), 278-82
CODEN: VIRLAX
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A significantly greater interferon prodn. has been obtained in primary rabbit **kidney** cell cultures exposed to poly(rI) followed by poly(rC) than in cell cultures exposed to poly(rC) followed by poly(rI). The interferon response in cell cultures

exposed to poly(rI) followed by poly(rC) was markedly more resistant to poly-**L-lysine** and pancreatic **RNase** treatment than was the interferon response in cell cultures exposed to poly(rC) followed by poly(rI). Poly-**L-lysine** treatment removed a substantially greater proportion of cell-assocd. radioactivity from cells exposed to [3H]poly(rC) followed by poly(rI) than from cells exposed to poly(rI) followed by [3H]-poly(rC). These findings suggest that the poly(rI).poly(rC) complex is more tightly and efficiently bound to the cell (surface) when the homopolymers are added in the order poly(rI), poly(rC) than when they are added in the order poly(rC), poly(rI) and that it is more effectively attached to the cell receptor site by its poly(rI) strand rather than by its poly(rC) strand.

(FILE 'CAPLUS' ENTERED AT 10:18:53 ON 09 MAY 2000)

L22 31825 SEA ABB=ON PLU=ON L17 OR RIBONUCLEASE OR ONCONASE OR (RIBONUCLEIC OR RIBO NUCLEIC)(1W)BIND?(W)PROTEIN OR RNASE

L23 242 SEA ABB=ON PLU=ON L22 AND (L3 OR (D OR L)(W)(LYSINE OR LYS))

L24 8 SEA ABB=ON PLU=ON L23 AND (KIDNEY OR RENAL?)

L25 0 SEA ABB=ON PLU=ON L24 NOT (L9 OR L20)

(FILE 'MEDLINE, BIOSIS, EMBASE, LIFESCI, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS' ENTERED AT 10:23:18 ON 09 MAY 2000)

L26 7 S L24

L27 7 S L26 NOT L10

L28 4 DUP REM L27 (3 DUPLICATES REMOVED)

L28 ANSWER 1 OF 4 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 82086433 EMBASE

DOCUMENT NUMBER: 1982086433

TITLE: Role of leukocyte factors and cationic polyelectrolytes in phagocytosis of group A streptococci and Candida albicans by neutrophils, macrophages, fibroblasts and epithelial cells: Modulation by anionic polyelectrolytes in relation to pathogenesis of chronic inflammation.

AUTHOR: Ginsburg I.; Sela M.N.; Morag A.; et al.

CORPORATE SOURCE: Dept. Oral Biol., Hebrew Univ. Hadassah Sch. Dent. Med., Jerusalem, Israel

SOURCE: Inflammation, (1981) 5/4 (289-312).
CODEN: INFLD4

COUNTRY: United States

DOCUMENT TYPE: Journal

FILE SEGMENT: 037 Drug Literature Index
026 Immunology, Serology and Transplantation
004 Microbiology
013 Dermatology and Venereology

Searcher : Shears 308-4994

LANGUAGE: English

AB A variety of cationic polyelectrolytes opsonized group A streptococci and Candida albicans to phagocytosis by human polymorphonuclear leukocytes and by mouse peritoneal macrophages. The most potent opsonins for streptococci were specific antibodies supplemented with complement, nuclear histone, polylysine, polyarginine, **ribonuclease**, leukocyte lysates, leukocyte cationic protein and, to a lesser extent, lysozyme and myeloperoxidase. Histone, **RNAse**, leukocyte extracts, and platelet extracts also functioned as opsonins for phagocytosis of streptococci in the peritoneal cavity, where phagocytic indices, higher than those obtained for the in vitro phagocytosis, were obtained. Fresh serum, polylysine, polyarginine, and nuclear histone acted as good opsonins for Candida, but none of the other factors tested were active. In order for the cationic proteins and leukocyte extracts to function as opsonins, they must be present on the particle surface. These agents were poor opsonins when applied on the macrophages. Nuclear histone, polylysine, polyarginine, and fresh human serum also functioned as good opsonins for the uptake of Candida by mouse fibroblasts. On the other hand, none of the other substances which opsonized streptococci were effective with Candida. The phagocytic capabilities of fibroblast polykaryons were much higher than those of ordinary spindle-shaped mouse fibroblasts. Histone also functioned as good opsonic agent for the uptake of Candida by human fibroblasts, HeLa cells, epithelial cells, monkey **kidney** cells, and rat heart cells. On the other hand, neither leukocyte extracts nor **ribonuclease** LCP or MPO functioned as opsonins for these mammalian cells. Candida, taken up by fibroblasts, were present within tight phagosomes, but no fusion of lysosomes with the phagosome occurred. A small proportion of the internalized yeast cells underwent partial plasmolysis, but little damage to the rigid cell walls was observed within 24-48 h of internalization. Phagocytosis of streptococci and Candida by macrophages and the uptake of Candida by fibroblasts were both strongly inhibited by liquoid (polyanethole sulfonic acid sodium salt). This anionic polyelectrolyte also markedly inhibited the release of N-acetylglucosaminidase from macropages without affecting cell viability (LDH release). Hyaluronic acid, DNA, and dextran sulfate markedly inhibited the uptake of histone-coated particles by macrophages. On the other hand, hyaluronic acid and DNA enhanced the uptake of Candida by fibroblasts. The effect of these anionic polyelectrolytes on phagocytosis of serum-opsonized particles by macrophages was not consistent. While in some experiments it blocked phagocytosis, in others it either had no effect or even enhanced the uptake of the particles. Phagocytosis of microorganisms by 'nonprofessional' phagocytes like fibroblasts and the paucity in these cells of hydrolases capable of breaking down microbial cell wall components may contribute to the persistence of nonbiodegradable components of bacteria in tissues and to the

perpetuation of chronic inflammatory sequellae. Cationic polyelectrolytes may also prove important as 'helper' opsonins and as agents capable of enhancing the pentration into cells of both viable and nonviable particles, genetic material, and drugs.

L28 ANSWER 2 OF 4 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 81246726 MEDLINE
DOCUMENT NUMBER: 81246726
TITLE: Inhibition of **renal** accumulation of lysozyme (basic low molecular weight protein) by basic proteins and other basic substances.
AUTHOR: Cojocel C; Franzen-Sieveking M; Beckmann G; Baumann K
SOURCE: PFLUGERS ARCHIV. EUROPEAN JOURNAL OF PHYSIOLOGY, (1981 Jun) 390 (3) 211-5.
Journal code: OZX. ISSN: 0031-6768.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198111

AB Together the two rat **kidneys** accumulated a total of 31.7 +/- 1.6% of the intravenously injected amount of 7 nmoles egg-white-lysozyme (measured as iodine 125 lysozyme) within 10 min. The low molecular weight protein lysozyme and other basic substances were injected simultaneously in order to evaluate whether these basic substances can inhibit the **renal** lysozyme accumulation. The inhibitory effect of various basic compounds was dose-dependent with a maximal reduction of lysozyme accumulation to 11.7 +/- 0.08%. The basic substances could be divided into three groups depending upon the micromolar amount injected at which a 50% inhibition was achieved (0.3-1.2 micromoles: cytochrome C, **ribonuclease**; 10.9 micromoles; spermine; 501-688 micromoles: L-arginine, **L-lysine**). The neutral myoglobin had no effect on **renal** lysozyme accumulation. The inhibitory potency appeared to increase with increasing molecular weight and pI value of the substance tested. Microperfusion experiments of proximal convoluted tubules of rat **kidney** revealed that luminal reabsorption of the basic lysozyme can be inhibited by the basic protein cytochrome C in a dose-dependent fashion. In these experiments the perfusion solution contained 57 micromol .l-1 lysozyme, an intratubular lysozyme concentration at which the tubular lysozyme reabsorption was found to be about 80% saturated. A 50% inhibition of the tubular endocytic lysozyme reabsorption was achieved a cytochrome C concentration of 102 micromol.l-1.

L28 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 2
ACCESSION NUMBER: 1977:227380 BIOSIS
DOCUMENT NUMBER: BA64:49744
TITLE: A RAT **KIDNEY** NEUTRAL PEPTIDASE THAT

DEGRADES B CHAIN OF INSULIN GLUCAGON AND ACTH PURIFICATION BY AFFINITY CHROMATOGRAPHY AND SOME PROPERTIES.

AUTHOR(S): VARANDANI P T; SHROYER L A

SOURCE: ARCH BIOCHEM BIOPHYS, (1977) 181 (1), 82-93.
CODEN: ABBIA4. ISSN: 0003-9861.
FILE SEGMENT: BA; OLD
LANGUAGE: Unavailable

AB A metallo-endopeptidase that catalyzes at near neutral pH the hydrolysis of certain polypeptides was purified from rat **kidney** microsomes by a simplified procedure using affinity chromatography on Sepharose 4B coupled with insulin B chain. The purified enzyme showed a single component by chromatography on diethylaminoethyl cellulose and by gel filtration on a Sephadex G-200 column. The native enzyme has a MW of approximately 213,000. Studies on its substrate specificity showed that the purified enzyme rapidly degrades insulin B chain, glucagon, ACTH, and, at a significantly lower rate, insulin A chain. The enzyme has a very weak or noaetivity toward **RNAse** and vasopressin. The enzyme does not degrade denatured Hb, bovine serum albumin, insulin (nano- or micromolar), oxytocin, furylacryloylglycyl-leucine amide (FAGLA), synthetic substrates of cathepsin C (.beta.-napthalamides of glycine-L-arginine and L-histidine-L-serine), or synthetic substrates of aminopeptidases (L-arginine- or L-glutamic acid-.beta.-naphthylamide). The enzyme degrades reduced or oxidized B chain at about the same rate, but S-sulfonated B chain is degraded at a markedly lower rate. The effect of several potential activators and inhibitors on the enzyme activity was investigated. Activity of the enzyme is markedly inhibited by chelating agents (EDTA and o-phenanthroline) and, modestly, by high concentrations of citrate and histidine. Activity of the enzyme is also markedly inhibited by simple thiol compounds (dithiothreitol, glutathione and mercaptoethanol), but not by sulfhydryl reagents (N-ethylmaleimide or iodoacetate). The inactive apoenzyme, prepared by treatment of the enzyme with EDTA followed by dialysis, was reactivated by Zn2+ > Ca2+, minimally by Cu2+, but not by Hg2+. Some anions (phosphate, borate and bicarbonate) were strongly inhibitory, but Cl had no effect. The following agents had no effect: soybean and lima bean trypsin inhibitors, N.rho.-tosyl-L-phenylalanine chloromethyl ketone (TPCK), N.alpha.,.rho.-tosyl-**L-lysine** chloromethyl ketone (TLCK), aprotinin (Trasylol), phenylmethylsulfonyl fluoride (a serine protease inhibitor), 1-methyl histidine, 3-methyl histidine, histamine, imidazole and heparin.

L28 ANSWER 4 OF 4 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 74049754 EMBASE
DOCUMENT NUMBER: 1974049754
TITLE: Poly(rI) more important than poly(rC) in the

interferon induction process by poly(rI)-poly(rC).

AUTHOR: De Clercq E.; Stewart II W.E.; De Somer P.
CORPORATE SOURCE: Rega Inst. Med. Res., Univ. Leuven, Belgium
SOURCE: Virology, (1973) 54/1 (278-282).
CODEN: VIRLAX
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
047 Virology
030 Pharmacology
LANGUAGE: English

AB A significantly greater interferon production has been obtained in primary rabbit **kidney** cell cultures exposed to poly(rI) followed by poly(rC) than in cell cultures exposed to poly(rC) followed by poly(rI). The interferon response in cell cultures exposed to poly(rI) followed by poly(rC) was markedly more resistant to poly **l lysine** and pancreatic **ribonuclease** treatment than was the interferon response in cell cultures exposed to poly(rC) followed by poly(rI). In addition, poly **l lysine** treatment removed a substantially greater proportion of cell associated radioactivity from cells exposed to [3H]poly(rC) followed by poly(rI) than from cells exposed to poly(rI) followed by [3H]poly(rC). These findings suggest that the poly(rI) poly(rC) complex is more tightly and efficiently bound to the cell (surface) when the homopolymers are added in the order poly(rI), poly(rC), than when they are added in the order poly(rC), poly(rI), and that it is more effectively attached to the cell receptor site by its poly(rI) strand than by its poly(rC) strand.

FILE 'USPATFULL' ENTERED AT 10:26:06 ON 09 MAY 2000

L1 (1) SEA FILE=REGISTRY ABB=ON PLU=ON D-LYSINE/CN
L2 (2) SEA FILE=REGISTRY ABB=ON PLU=ON POLY-L-LYSINE/CN
L3 3 SEA FILE=REGISTRY ABB=ON PLU=ON L1 OR L2
L13 37 SEA FILE=USPATFULL ABB=ON PLU=ON (L3 OR (L OR D)(W)(LYSINE OR LYS))(L)((KIDNEY OR RENAL?)(5A)(UPTAK? OR RETENT?))
L14 28 SEA FILE=USPATFULL ABB=ON PLU=ON L13(L)ADMIN?
L15 1 SEA FILE=REGISTRY ABB=ON PLU=ON ONCONASE/CN
L16 215 SEA FILE=REGISTRY ABB=ON PLU=ON RIBONUCLEASE ?/CN
L17 216 SEA FILE=REGISTRY ABB=ON PLU=ON L15 OR L16
L22 31825 SEA FILE=CAPLUS ABB=ON PLU=ON L17 OR RIBONUCLEASE OR ONCONASE OR (RIBONUCLEIC OR RIBO NUCLEIC)(1W)BIND?(W)PROTEIN OR RNASE
L31 641 SEA FILE=USPATFULL ABB=ON PLU=ON L22(L)(L3 OR (D OR L)(W)(LYSINE OR LYS))
L32 284 SEA FILE=USPATFULL ABB=ON PLU=ON L31(L)(RENAL? OR KIDNEY)
L33 91 SEA FILE=USPATFULL ABB=ON PLU=ON L32(L)(ADMIN?(5A)(ORAL? OR MOUTH OR PER OS))
L34 54 SEA FILE=USPATFULL ABB=ON PLU=ON L33(L)(KD? OR KILOD?

Searcher : Shears 308-4994

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               OR KILO(W)(D OR DALT?))
L35          20 SEA FILE=USPATFULL ABB=ON  PLU=ON  L34(L)ISOTOP?
L36          20 SEA FILE=USPATFULL ABB=ON  PLU=ON  L35 NOT L14

=> d 1-20 .bevpat

L36  ANSWER 1 OF 20  USPATFULL
ACCESSION NUMBER:        2000:18558  USPATFULL
TITLE:                   Multidrug resistance proteins
INVENTOR(S):             Deeley, Roger G., Kingston, Canada
                         Cole, Susan P. C., Kingston, Canada
PATENT ASSIGNEE(S):      Queen's University at Kingston, Kingston, Canada
                         (non-U.S. corporation)

                              NUMBER         DATE
                         ---------------- --------
PATENT INFORMATION:      US 6025473       20000215
APPLICATION INFO.:       US 1995-461384   19950605  (8)
RELATED APPLN. INFO.:    Continuation-in-part of Ser. No. US 1995-407207,
                         filed on 20 Mar 1995 which is a
                         continuation-in-part of Ser. No. US 1993-141893,
                         filed on 26 Oct 1993, now patented, Pat. No. US
                         5489519 which is a continuation-in-part of Ser.
                         No. US 1993-29340, filed on 8 Mar 1993, now
                         abandoned which is a continuation-in-part of Ser.
                         No. US 1992-966923, filed on 27 Oct 1992, now
                         abandoned
DOCUMENT TYPE:           Utility
PRIMARY EXAMINER:        Burke, Julie
LEGAL REPRESENTATIVE:    Steeg, Carol Miernicki; Kara, Catherine J.;
                         DeConti, Jr., Giulio A.
NUMBER OF CLAIMS:        19
EXEMPLARY CLAIM:         1
NUMBER OF DRAWINGS:      23 Drawing Figure(s); 21 Drawing Page(s)
LINE COUNT:              4915
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB       A novel protein associated with multidrug resistance in living
         cells and capable of conferring multidrug resistance on a cell is
         disclosed. Nucleic acids encoding the novel multidrug resistance
         protein are also disclosed. Transformant cell lines which express
         the nucleic acid encoding the novel protein are also disclosed.
         Antibodies which bind the novel multidrug resistance protein are
         also disclosed. Diagnostic and treatment methods using the novel
         proteins, nucleic acids, antibodies and cell lines of the
         invention are also encompassed by the invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL     INCLM: 530/350.000
         INCLS: 530/300.000; 530/395.000; 536/023.500; 514/012.000;
                              Searcher   :    Shears   308-4994
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435/183.000
NCL NCLM: 530/350.000
NCLS: 435/183.000; 530/300.000; 530/395.000; 536/023.500

L36 ANSWER 2 OF 20 USPATFULL
ACCESSION NUMBER: 2000:7057 USPATFULL
TITLE: Transferrin receptor specific antibody-neuropharmaceutical or diagnostic agent conjugates
INVENTOR(S): Friden, Phillip M., Bedford, MA, United States
PATENT ASSIGNEE(S): Alkermes, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6015555	20000118
APPLICATION INFO.:	US 1995-444644	19950519 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 232246	

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Burke, Julie
LEGAL REPRESENTATIVE: Hamilton, Brook, Smith & Reynolds, P.C.
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 79 Drawing Figure(s); 77 Drawing Page(s)
LINE COUNT: 3966
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention pertains to a method for delivering a neuropharmaceutical or diagnostic agent across the blood brain barrier to the brain of a host. The method comprises administering to the host a therapeutically effective amount of an antibody-neuropharmaceutical or diagnostic agent conjugate wherein the antibody is reactive with a transferrin receptor and the antibody is a chimera between the variable region from one animal source and the constant region from a different animal source. Other aspects of this invention include a delivery system comprising an antibody reactive with a transferrin receptor linked to a neuropharmaceutical or diagnostic agent and methods for treating hosts afflicted with a disease associated with a neurological disorder.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/133.100
INCLS: 530/387.300; 530/388.220; 424/143.100; 435/007.210; 435/069.600; 435/069.700; 435/328.000; 435/334.000
NCL NCLM: 424/133.100
NCLS: 424/143.100; 435/007.210; 435/069.600; 435/069.700; 435/328.000; 435/334.000; 530/387.300; 530/388.220

L36 ANSWER 3 OF 20 USPATFULL

ACCESSION NUMBER:	1999:170413 USPATFULL
TITLE:	Brain-associated inhibitor of tissue-type plasminogen activator
INVENTOR(S):	Hastings, Gregg A., Thousand Oaks, CA, United States Coleman, Timothy A., Gaithersburg, MD, United States Lawrence, Daniel A., Derwood, MD, United States Dillon, Patrick J., Carlsbad, CA, United States
PATENT ASSIGNEE(S):	Human Genome Sciences, Rockville, MD, United States (U.S. corporation) The American Red Cross, Falls Church, VA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6008020	19991228
APPLICATION INFO.:	US 1997-948997	19971010 (8)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1996-28117	19961011 (60)

DOCUMENT TYPE:	Utility
PRIMARY EXAMINER:	Achutamurthy, Ponnathapura
ASSISTANT EXAMINER:	Slobodyansky, Elizabeth
LEGAL REPRESENTATIVE:	Wales, Michele M.
NUMBER OF CLAIMS:	43
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	8 Drawing Figure(s); 10 Drawing Page(s)
LINE COUNT:	3654

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a novel BAIT protein which is a member of serpin superfamily which is expressed primarily in brain tissue. In particular, isolated nucleic acid molecules are provided encoding the human BAIT protein. BAIT polypeptides are also provided as are vectors, host cells and recombinant methods for producing the same. The invention further relates to screening methods for identifying agonists and antagonists of BAIT activity. Also provided are diagnostic methods for detecting nervous system-related disorders and therapeutic methods for treating nervous system-related disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 435/069.200
INCLS: 435/069.700; 435/252.300; 435/320.100; 435/325.000; 536/023.100; 536/023.500

NCL NCLM: 435/069.200
NCLS: 435/069.700; 435/252.300; 435/320.100; 435/325.000; 536/023.100; 536/023.500

Searcher : Shears 308-4994

L36 ANSWER 4 OF 20 USPATFULL
ACCESSION NUMBER: 1999:170407 USPATFULL
TITLE: Method of making lipid metabolic pathway compositions
INVENTOR(S): Gimeno, Carlos J., Boston, MA, United States
Acton, Susan, Jamaica Plain, MA, United States
PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6008014	19991228
APPLICATION INFO.:	US 1996-707399	19960904 (8)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Burke, Julie
LEGAL REPRESENTATIVE: Lahive & Cockfield, LLP; Mandragouras, Amy E.
NUMBER OF CLAIMS: 29
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 4 Drawing Page(s)
LINE COUNT: 4049
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to the discovery of novel genes encoding Lipid Metabolic Pathway (LMP) polypeptides. Therapeutics, diagnostics and screening assays based on these molecules are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/069.100
INCLS: 435/091.100; 435/455.000; 435/325.000; 536/023.100
NCL NCLM: 435/069.100
NCLS: 435/091.100; 435/325.000; 435/455.000; 536/023.100

L36 ANSWER 5 OF 20 USPATFULL
ACCESSION NUMBER: 1999:163419 USPATFULL
TITLE: Methods for identifying chemosensitizers
INVENTOR(S): Deeley, Roger G., Kingston, Canada
Cole, Susan P.C., Kingston, Canada
PATENT ASSIGNEE(S): Queen's University at Kingston, Kingston, Canada (non-U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 6001563	19991214
APPLICATION INFO.:	US 1995-463179	19950605 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1995-407207, filed on 20 Mar 1995 which is a continuation-in-part of Ser. No. US 1993-141893, filed on 26 Oct 1993, now patented, Pat. No. US

5489519, issued on 6 Feb 1996 which is a continuation-in-part of Ser. No. US 1993-29340, filed on 8 Mar 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-966923, filed on 27 Oct 1992, now abandoned

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Stanton, Brian R.
ASSISTANT EXAMINER: Clark, Deborah J. R.
LEGAL REPRESENTATIVE: Steeg, Carol Miernicki; Kara, Catherine J.; DeConti, Jr., Giulio A.
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1,7
NUMBER OF DRAWINGS: 13 Drawing Figure(s); 21 Drawing Page(s)
LINE COUNT: 4885
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A novel protein associated with multidrug resistance in living cells and capable of conferring multidrug resistance on a cell is disclosed. Nucleic acids encoding the novel multidrug resistance protein are also disclosed. Transformant cell lines which express the nucleic acid encoding the novel protein are also disclosed. Antibodies which bind the novel multidrug resistance protein are also disclosed. Diagnostic and treatment methods using the novel proteins, nucleic acids, antibodies and cell lines of the invention are also encompassed by the invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/006.000
INCLS: 435/325.000; 435/006.000; 435/004.000; 435/029.000; 800/002.000; 800/DIG.0014; 800/013.000; 424/009.100
NCL NCLM: 435/006.000
NCLS: 424/009.100; 435/004.000; 435/029.000; 435/325.000; 800/013.000

L36 ANSWER 6 OF 20 USPATFULL
ACCESSION NUMBER: 1999:155454 USPATFULL
TITLE: Trio molecules and uses related thereto
INVENTOR(S): Streuli, Michel, Brookline, MA, United States
Debant, Anne, Padres le Lez, France
Serra-Pages, Carles, Boston, MA, United States
PATENT ASSIGNEE(S): Dana-Farber Cancer Institute, Boston, MA, United States (U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 5994070	19991130	
APPLICATION INFO.:	US 1997-826267	19970327	(8)

	NUMBER	DATE
Searcher :	Shears	308-4994

PRIORITY INFORMATION: US 1996-14214 19960327 (60)
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Campell, Bruce R.
LEGAL REPRESENTATIVE: Lahive & Cockfield, LLP; Mandragouras, Amy E.; Williams, Megan E.
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 50 Drawing Figure(s); 27 Drawing Page(s)
LINE COUNT: 4596
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Nucleic acids encoding TRIO proteins, the TRIO proteins themselves, and active portions thereof as described. In addition, antibodies immunoreactive with TRIO proteins, and preparations of such compositions are provided. Diagnostic and therapeutic assays and reagents for detecting and treating disorders involving, for example, aberrant expression (or loss thereof) of the TRIO protein are described. Assays are provided for identifying agents that modulate the biological function of TRIO proteins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/006.000
INCLS: 435/069.100; 435/320.100; 435/325.000; 536/023.500; 536/024.310
NCL NCLM: 435/006.000
NCLS: 435/069.100; 435/320.100; 435/325.000; 536/023.500; 536/024.310

L36 ANSWER 7 OF 20 USPATFULL
ACCESSION NUMBER: 1999:146285 USPATFULL
TITLE: Processes using a human serotonin receptor (5-HT.sub.4B)
INVENTOR(S): Bard, Jonathan A., Wyckoff, NJ, United States
Branchek, Theresa, Teaneck, NJ, United States
Weinshank, Richard L., New York, NY, United States
PATENT ASSIGNEE(S): Synaptic Pharmaceutical Coorporation, Paramus, NJ, United States (U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 5985585	19991116	
	WO 9409828	19940511	
APPLICATION INFO.:	US 1995-157185	19950615	(8)
	WO 1993-US10553	19931029	
		19950615	PCT 371 date
		19950615	PCT 102(e) date

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1992-971690, filed on 3 Nov 1992, now abandoned And Ser. No. US 1994-281526, filed on 27 Jul 1994
Searcher : Shears 308-4994

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Allen, Marianne P.
LEGAL REPRESENTATIVE: White, John P.Cooper & Dunham LLP
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 12 Drawing Figure(s); 12 Drawing Page(s)
LINE COUNT: 2704
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides for processes for identifying chemical compounds which specifically bind to a human 5-HT.sub.4B having the amino acid sequence of SEQ ID NO: 2.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/007.210
INCLS: 435/325.000; 435/356.000; 435/357.000; 435/358.000; 435/365.000
NCL NCLM: 435/007.210
NCLS: 435/325.000; 435/356.000; 435/357.000; 435/358.000; 435/365.000

L36 ANSWER 8 OF 20 USPATFULL
ACCESSION NUMBER: 1999:75310 USPATFULL
TITLE: Methods of treating TNF.alpha.-mediated disease using chimeric anti-TNF antibodies
INVENTOR(S): Le, Junming, Jackson Heights, NY, United States
Vilcek, Jan, New York, NY, United States
Dadonna, Peter, Palo Alto, CA, United States
Ghrayeb, John, Thorndale, PA, United States
Knight, David, Berwyn, PA, United States
Seigal, Scott, Westborough, MA, United States
PATENT ASSIGNEE(S): New York University, New York, NY, United States (U.S. corporation)
Centocor, Inc., Malvern, PA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5919452	19990706
APPLICATION INFO.:	US 1994-192861	19940204 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1993-10406, filed on 29 Jan 1993, now abandoned And Ser. No. US 1993-13413, filed on 2 Feb 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-943852, filed on 11 Sep 1992, now abandoned which is a continuation-in-part of Ser. No. US 1992-853606, filed on 18 Mar 1992, now abandoned which is a continuation-in-part of Ser. No. US 1991-670827, filed on 18 Mar 1991, now abandoned
DOCUMENT TYPE: Utility
Searcher : Shears 308-4994

PRIMARY EXAMINER: Scheiner, Toni R.
ASSISTANT EXAMINER: Johnson, Nancy A.
LEGAL REPRESENTATIVE: Hamilton, Brook, Smith & Reynolds, P.C.
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 48 Drawing Figure(s); 36 Drawing Page(s)
LINE COUNT: 5351
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Treatment of tumor necrosis factor, TNF, mediated pathologies is provided by administering anti-TNF compounds, such as anti-TNF antibodies and anti-TNF peptides, which compounds are specific for tumor necrosis factor-.alpha. (TNF.alpha.) or tumor necrosis factor-.beta. (TNF.beta.) and which are useful for in vivo therapy or diagnosis of TNF.alpha.-mediated pathologies and conditions, wherein the anti-TNF compound is selected from the group consisting of at least one of an immunoglobulin variable region, a fragment of a TNF receptor and an anti-TNF peptide, such as a structural analog of a anti-TNF antibody fragment or a TNF receptor fragment.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/133.100
INCLS: 424/145.100; 424/158.100; 530/387.300; 530/388.230; 530/389.200
NCL NCLM: 424/133.100
NCLS: 424/145.100; 424/158.100; 530/387.300; 530/388.230; 530/389.200

L36 ANSWER 9 OF 20 USPATFULL
ACCESSION NUMBER: 1999:43471 USPATFULL
TITLE: Methods for conferring multidrug resistance on a cell
INVENTOR(S): Deeley, Roger G., Kingston, Canada
Cole, Susan P. C., Kingston, Canada
PATENT ASSIGNEE(S): Queen's University at Kingston, Kingston, Canada (non-U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5891724	19990406
APPLICATION INFO.:	US 1995-460907	19950605 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1995-407207, filed on 20 Mar 1995 which is a continuation-in-part of Ser. No. US 1993-141893, filed on 26 Oct 1993, now patented, Pat. No. US 5489519, issued on 6 Feb 1996 which is a continuation-in-part of Ser. No. US 1993-29340, filed on 8 Mar 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-966923,

filed on 27 Oct 1992, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: LaGuyader, John L.
ASSISTANT EXAMINER: Schwartzman, Robert
LEGAL REPRESENTATIVE: Steeg, Carol Mlernicki; Kara, Catherine J.; DeConti, Jr., Giulio A.
NUMBER OF CLAIMS: 21
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 26 Drawing Figure(s); 21 Drawing Page(s)
LINE COUNT: 4215
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A novel protein associated with multidrug resistance in living cells and capable of conferring multidrug resistance on a cell is disclosed. Nucleic acids encoding the novel multidrug resistance protein are also disclosed. Transformant cell lines which express the nucleic acid encoding the novel protein are also disclosed. Antibodies which bind the novel multidrug resistance protein are also disclosed. Diagnostic and treatment methods using the novel proteins, nucleic acids, antibodies and cell lines of the invention are also encompassed by the invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/375.000
INCLS: 435/006.000; 435/069.100; 435/172.300; 435/320.100; 435/325.000; 435/367.000; 536/023.100; 536/023.500
NCL NCLM: 435/375.000
NCLS: 435/006.000; 435/069.100; 435/320.100; 435/325.000; 435/367.000; 435/456.000; 536/023.100; 536/023.500

L36 ANSWER 10 OF 20 USPATFULL
ACCESSION NUMBER: 1999:43412 USPATFULL
TITLE: Vectors and methods for recombinant production of uPA-binding fragments of the human urokinase-type plasminogen receptor (uPAR)
INVENTOR(S): Dan.o slashed. , Keld, Charlottenlund, Denmark
Blasi, Francesco, Charlottenlund, Denmark
Roldan, Ann Louring, Vallensb.ae butted.k, Denmark
Cubellis, Maria Vittoria, Napoli, Italy
Masucci, Maria Teresa, Napoli, Italy
Appella, Ettore, Chevy Chase, MD, United States
Schleuning, Wolf-Dieter, Berlin, Germany, Federal Republic of
Behrendt, Niels, Bagsv.ae butted.rd, Denmark
R.o slashed.nne, Ebbe, Copenhagen, Denmark
Kristensen, Peter, Copenhagen, Denmark
Pollanen, Jari, Espoo, Finland
Salonen, Eeva-Marjatta, Espoo, Finland
Stephens, Ross W., Helsinki, Finland
Searcher : Shears 308-4994

Tapiovaara, Hannele, Helsinki, Finland
Vaheri, Antti, Kauniainen, Finland
M.o slashed.ller, Lisbeth Birk, Bagsv.ae butted.rd, Denmark
Ellis, Vincent, Copenhagen, Denmark
Lund, Leif R.o slashed.ge, Copenhagen, Denmark
Ploug, Michael, Copenhagen, Denmark
Pyke, Charles, S.o slashed.borg, Denmark
Patthy, Laszlo, Budapest, Hungary
PATENT ASSIGNEE(S): Cancerforskningsfondet af 1989, Copenhagen K, Denmark (non-U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5891664	19990406
APPLICATION INFO.:	US 1994-319052	19941006 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1991-824189, filed on 6 Dec 1991, now abandoned which is a continuation-in-part of Ser. No. US 1989-374854, filed on 3 Jul 1989, now abandoned which is a continuation-in-part of Ser. No. US 1989-334613, filed on 7 Apr 1989, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Walsh, Stephen G.
ASSISTANT EXAMINER: Fitzgerald, David L.
LEGAL REPRESENTATIVE: Cooper, Iver P.
NUMBER OF CLAIMS: 22
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 83 Drawing Figure(s); 53 Drawing Page(s)
LINE COUNT: 6449
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Activation of plasminogen to plasma is inhibited by preventing the binding of a receptor binding form of urokinase-type plasminogen activator to a urokinase-type plasminogen activator receptor in a mammal, thereby preventing the urokinase-type plasminogen activator from converting plasminogen into plasmin. DNA fragments which encode for soluble, active fragments of the urokinase-type plasminogen activator are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/069.100
INCLS: 435/320.100; 435/069.700; 536/023.500
NCL NCLM: 435/069.100
NCLS: 435/069.700; 435/320.100; 536/023.500

L36 ANSWER 11 OF 20 USPATFULL
ACCESSION NUMBER: 1999:36949 USPATFULL
TITLE: Engineering oral tissues
INVENTOR(S): Mooney, David J., Ann Arbor, MI, United States
Searcher : Shears 308-4994

	Rutherford, Robert B., Ann Arbor, MI, United States
PATENT ASSIGNEE(S):	The Regents of the University of Michigan, Ann Arbor, MI, United States (U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 5885829	19990323	
APPLICATION INFO.:	US 1997-864494	19970528	(8)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 1996-18450	19960528	(60)

DOCUMENT TYPE:	Utility
PRIMARY EXAMINER:	Degen, Nancy
LEGAL REPRESENTATIVE:	Arnold, White & Durkee
NUMBER OF CLAIMS:	109
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	17 Drawing Figure(s); 11 Drawing Page(s)
LINE COUNT:	8001

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are methods for regenerating dental and oral tissues from viable cells using ex vivo culture on a structural matrix. The regenerated oral tissues and tissue-matrix preparations thus provided have both clinical applications in dentistry and oral medicine and are also useful in in vitro toxicity and biocompatibility testing.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 435/325.000
INCLS: 424/049.000; 424/422.000; 424/435.000; 435/069.500; 435/374.000; 435/378.000

NCL NCLM: 435/325.000
NCLS: 424/049.000; 424/422.000; 424/435.000; 435/069.100; 435/374.000; 435/378.000

L36 ANSWER 12 OF 20 USPATFULL

ACCESSION NUMBER:	1999:33784 USPATFULL
TITLE:	Methods for identifying multidrug resistant tumor cells
INVENTOR(S):	Deeley, Roger G., Kingston, Canada Cole, Susan P. C., Kingston, Canada
PATENT ASSIGNEE(S):	Queen's University at Kingston, Kingston, Canada (non-U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 5882875	19990316	
APPLICATION INFO.:	US 1995-462109	19950605	(8)

Searcher : Shears 308-4994

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1995-407207, filed on 20 Mar 1995 which is a continuation-in-part of Ser. No. US 1993-141893, filed on 26 Oct 1993, now patented, Pat. No. US 5489519, issued on 6 Feb 1996 which is a continuation-in-part of Ser. No. US 1993-29340, filed on 8 Mar 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-966923, filed on 27 Oct 1992, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Huff, Sheela
ASSISTANT EXAMINER: Reeves, Julie E
LEGAL REPRESENTATIVE: Steeg, Carol Miernicki; Kara, Catherine J.; DeConti, Jr., Giulio A.
NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 26 Drawing Figure(s); 21 Drawing Page(s)
LINE COUNT: 4149
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A novel protein associated with multidrug resistance in living cells and capable of conferring multidrug resistance on a cell is disclosed. Nucleic acids encoding the novel multidrug resistance protein are also disclosed. Transformant cell lines which express the nucleic acid encoding the novel protein are also disclosed. Antibodies which bind the novel multidrug resistance protein are also disclosed. Diagnostic and treatment methods using the novel proteins, nucleic acids, antibodies and cell lines of the invention are also encompassed by the invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/007.230
INCLS: 424/155.100; 530/388.800
NCL NCLM: 435/007.230
NCLS: 424/155.100; 530/388.800

L36 ANSWER 13 OF 20 USPATFULL
ACCESSION NUMBER: 1999:12769 USPATFULL
TITLE: Nucleic acid encoding novel receptor-type phosphotyrosine phosphatase-.kappa.
INVENTOR(S): Schlessinger, Joseph, New York, NY, United States
Sap, Jan M., New York, NY, United States
Ullrich, Axel, Munchen, Germany, Federal Republic of
Vogel, Wolfgang, Germering, Germany, Federal Republic of
Fuchs, Miriam, Starnberg, Germany, Federal Republic of
PATENT ASSIGNEE(S): Max Planck Gessellschaft, Gottingen, Germany, Federal Republic of (non-U.S. corporation)

New York University Medical Center, New York, NY, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5863755	19990126
APPLICATION INFO.:	US 1993-87244	19930701 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1993-49384, filed on 21 Apr 1993, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Teng, Sally
LEGAL REPRESENTATIVE: Pennie & Edmonds LLP
NUMBER OF CLAIMS: 19
EXEMPLARY CLAIM: 4
NUMBER OF DRAWINGS: 49 Drawing Figure(s); 37 Drawing Page(s)
LINE COUNT: 3616
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A novel receptor-type protein tyrosine phosphatase-.kappa. (RPTP.kappa.) protein or glycoprotein and the DNA coding therefor is expressed in a wide variety of mammalian tissues. The RPTP.kappa. protein or glycoprotein may be produced by recombinant means. Antibodies to the protein, methods for measuring the quantity of the protein, methods for screening compounds, such as drugs, which can bind to the protein and inhibit or stimulate their enzymatic activity, are provided. Further, methods for inhibiting homophilic binding of Type II RPTP, especially RPTP.kappa. molecules are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/069.100
INCLS: 435/252.300; 435/254.110; 435/320.100; 435/325.000; 435/196.000; 536/023.500; 536/024.310
NCL NCLM: 435/069.100
NCLS: 435/196.000; 435/252.300; 435/254.110; 435/320.100; 435/325.000; 536/023.500; 536/024.310

L36 ANSWER 14 OF 20 USPATFULL
ACCESSION NUMBER: 1999:1500 USPATFULL
TITLE: Receptor-type phosphotyrosine phosphatase-.kappa.
INVENTOR(S): Schlessinger, Joseph, New York, NY, United States
Sap, Jan M., New York, NY, United States
Ullrich, Axel, Munchen, Germany, Federal Republic of
Vogel, Wolfgang, Germering, Germany, Federal Republic of
Fuchs, Miriam, Starnberg, Germany, Federal Republic of
PATENT ASSIGNEE(S): New York University Medical Center, New York, NY, United States (U.S. corporation)
Searcher : Shears 308-4994

	NUMBER	DATE
PATENT INFORMATION:	US 5856162	19990105
APPLICATION INFO.:	US 1995-449644	19950524 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1993-87244, filed on 1 Jul 1993 which is a continuation-in-part of Ser. No. US 1993-49384, filed on 21 Apr 1993, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Teng, Sally P.
LEGAL REPRESENTATIVE: Pennie & Edmonds LLP
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 2,4
NUMBER OF DRAWINGS: 49 Drawing Figure(s); 37 Drawing Page(s)
LINE COUNT: 3605
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A novel receptor-type protein tyrosine phosphatase-.kappa. (RPTP.kappa.) protein or glycoprotein and the DNA coding therefor is expressed in a wide variety of mammalian tissues. The RPTP.kappa. protein or glycoprotein may be produced by recombinant means. Antibodies to the protein, methods for measuring the quantity of the protein, methods for screening compounds, such as drugs, which can bind to the protein and inhibit or stimulate their enzymatic activity, are provided. Further, methods for inhibiting homophilic binding of Type II RPTP, especially RPTP.kappa. molecules are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/196.000
INCLS: 435/069.100; 435/069.700; 536/023.500; 530/350.000
NCL NCLM: 435/196.000
NCLS: 435/069.100; 435/069.700; 530/350.000; 536/023.500

L36 ANSWER 15 OF 20 USPATFULL
ACCESSION NUMBER: 1998:115581 USPATFULL
TITLE: Hybrid immunoglobulin-thrombolytic enzyme molecules which specifically bind a thrombus, and methods of their production and use
INVENTOR(S): Quertermous, Thomas, Nashville, TN, United States
Runge, Marschall Stevens, Atlanta, GA, United States
Haber, Edgar, Salisbury, NH, United States
PATENT ASSIGNEE(S): The General Hospital Corporation, Boston, MA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5811265	19980922

Searcher : Shears 308-4994

APPLICATION INFO.: US 0961736 19930726 (8)
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. 2861, filed on 15 Jan 1993, now abandoned And a continuation-in-part of Ser. No. 589435, filed on 27 Sep 1990, now abandoned which is a continuation-in-part of Ser. No. 435485, filed on 7 Jul 1989, now abandoned , said Ser. No. 2861 which is a continuation of Ser. No. 234051, filed on 19 Aug 1988, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Nucker, Christine M.
ASSISTANT EXAMINER: Scheiner, Laurie
LEGAL REPRESENTATIVE: Sterne, Kessler, Goldstein & Fox P.L.L.C.
NUMBER OF CLAIMS: 6
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 31 Drawing Figure(s); 33 Drawing Page(s)
LINE COUNT: 4098
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Hybrid immunoglobulin-enzyme molecules are provided which are composed of antibodies, or derivatives or fragments thereof, which specifically bind an arterial or venous thrombus that are operably linked to the enzymatically active portions of thrombolytic enzymes such as plasminogen activators. In a preferred embodiment the hybrid molecules specifically bind to fibrin and have fibrinolytic activity. The hybrid molecules of the present invention may be produced by any means, including chemical conjugation, or by means of recombinant DNA, genetic engineering and/or hybridoma technology. Methods for making and using the molecules in diagnosis and therapy are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/069.300
INCLS: 435/172.200; 435/172.300; 435/252.300; 536/023.400; 536/023.530
NCL NCLM: 435/069.300
NCLS: 435/252.300; 536/023.400; 536/023.530

L36 ANSWER 16 OF 20 USPATFULL
ACCESSION NUMBER: 1998:68805 USPATFULL
TITLE: Isolated nucleic acid molecules encoding multidrug resistance proteins
INVENTOR(S): Deeley, Roger G., Kingston, Canada
Cole, Susan P.C., Kingston, Canada
PATENT ASSIGNEE(S): Queen's University at Kingston, Kingston, Canada (non-U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5766880	19980616

Searcher : Shears 308-4994

APPLICATION INFO.: US 1995-463092 19950605 (8)
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1995-407207, filed on 20 Mar 1995 which is a continuation-in-part of Ser. No. US 1993-141893, filed on 26 Oct 1993, now patented, Pat. No. US 5489519, issued on 6 Feb 1996 which is a continuation-in-part of Ser. No. US 1993-29340, filed on 8 Mar 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-966923, filed on 27 Oct 1992, now abandoned
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Elliott, George C.
ASSISTANT EXAMINER: Schwarteman, Robert
LEGAL REPRESENTATIVE: Steeg, Carol Miernicki; Kara, Catherine J.; DeConti, Jr., Giulio A.
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 30 Drawing Figure(s); 21 Drawing Page(s)
LINE COUNT: 3632
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A novel protein associated with multidrug resistance in living cells and capable of conferring multidrug resistance on a cell is disclosed. Nucleic acids encoding the novel multidrug resistance protein are also disclosed. Transformant cell lines which express the nucleic acid encoding the novel protein are also disclosed. Antibodies which bind the novel multidrug resistance protein are also disclosed. Diagnostic and treatment methods using the novel proteins, nucleic acids, antibodies and cell lines of the invention are also encompassed by the invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 435/069.100
INCLS: 435/243.000; 435/320.100; 435/366.000; 435/372.000; 536/023.500; 536/024.310
NCL NCLM: 435/069.100
NCLS: 435/243.000; 435/320.100; 435/366.000; 435/372.000; 536/023.500; 536/024.310

L36 ANSWER 17 OF 20 USPATFULL
ACCESSION NUMBER: 97:117693 USPATFULL
TITLE: Methods of treating rheumatoid arthritis using chimeric anti-TNF antibodies
INVENTOR(S): Le, Junming, Jackson Heights, NY, United States
Vilcek, Jan, New York, NY, United States
Daddona, Peter, Menlo Park, CA, United States
Ghrayeb, John, Thorndale, PA, United States
Knight, David, Berwyn, PA, United States
Siegel, Scott, Westborough, MA, United States
PATENT ASSIGNEE(S): New York University Medical Center, New York, NY,

United States (U.S. corporation)
Centocor, Inc., Malvern, PA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5698195	19971216
APPLICATION INFO.:	US 1994-324799	19941018 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1994-192102, filed on 4 Feb 1994 Ser. No. Ser. No. US 1994-192061, filed on 4 Feb 1994, now abandoned And Ser. No. US 1994-192093, filed on 4 Feb 1994, now abandoned , each Ser. No. US - which is a continuation-in-part of Ser. No. US 1993-10406, filed on 29 Jan 1993, now abandoned And Ser. No. US 1993-13413, filed on 2 Feb 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-943852, filed on 11 Sep 1992, now abandoned which is a continuation-in-part of Ser. No. US 1992-853606, filed on 18 Mar 1992, now abandoned which is a continuation-in-part of Ser. No. US 1991-670827, filed on 18 Mar 1991, now abandoned

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Feisee, Lila
ASSISTANT EXAMINER: Lucas, John
LEGAL REPRESENTATIVE: Hamilton, Brook, Smith & Reynolds, P.C.
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 33 Drawing Figure(s); 36 Drawing Page(s)
LINE COUNT: 5887

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Anti-TNF antibodies, fragments and regions thereof which are specific for human tumor necrosis factor-.alpha. (TNF.alpha.) and are useful in vivo for diagnosis and therapy of a number of TNF.alpha.-mediated pathologies and conditions, including rheumatoid arthritis as well as polynucleotides coding for murine and chimeric antibodies, methods of producing the antibody, methods of use of the anti-TNF antibody, or fragment, region or derivative thereof, in immunoassays and immunotherapeutic approaches are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 424/133.100
INCLS: 424/141.100; 424/145.100; 424/192.100; 514/825.000; 530/387.300; 530/388.100; 530/388.230; 530/351.000
NCL NCLM: 424/133.100
NCLS: 424/141.100; 424/142.100; 424/145.100; 514/825.000; 530/351.000; 530/387.300; 530/388.100; 530/388.230

L36 ANSWER 18 OF 20 USPATFULL

ACCESSION NUMBER: 97:70718 USPATFULL

TITLE: Methods of treating TNF-.alpha.-mediated Crohn's disease using chimeric anti-TNF antibodies

INVENTOR(S): Le, Junming, Jackson Heights, NY, United States
Vilcek, Jan, New York, NY, United States
Dadonna, Peter, Palo Alto, CA, United States
Ghrayeb, John, Thorndale, PA, United States
Knight, David, Berwyn, PA, United States
Siegel, Scott A., Westborough, MA, United States

PATENT ASSIGNEE(S): New York University Medical Center, New York, NY, United States (U.S. corporation)
Centocor, Inc., Malvern, PA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5656272	19970812
APPLICATION INFO.:	US 1994-192102	19940204 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1993-10406, filed on 26 Jan 1993, now abandoned And Ser. No. US 1993-13413, filed on 2 Feb 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-943852, filed on 11 Sep 1992, now abandoned which is a continuation-in-part of Ser. No. US 1992-853606, filed on 18 Mar 1992, now abandoned which is a continuation-in-part of Ser. No. US 1991-670827, filed on 18 Mar 1991, now abandoned

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Feisee, Lila
ASSISTANT EXAMINER: Lucas, John
LEGAL REPRESENTATIVE: Hamilton, Brook, Smith & Reynolds, P.C.
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 48 Drawing Figure(s); 36 Drawing Page(s)
LINE COUNT: 5251

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Anti-TNF antibodies, fragments and regions thereof which are specific for human tumor necrosis factor-.alpha. (TNF.alpha.) and are useful in vivo for diagnosis and therapy of a number of TNF.alpha.-mediated pathologies and conditions, including Crohn's disease, as well as polynucleotides coding for murine and chimeric antibodies, methods of producing the antibody, methods of use of the anti-TNF antibody, or fragment, region or derivative thereof, in immunoassays and immunotherapeutic approaches are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

INCL INCLM: 424/133.100
INCLS: 424/145.100; 424/139.100; 435/069.100; 435/069.600;

435/069.700; 530/387.300; 530/388.230
NCL NCLM: 424/133.100
NCLS: 424/139.100; 424/145.100; 435/069.100; 435/069.600;
435/069.700; 530/387.300; 530/388.230

L36 ANSWER 19 OF 20 USPATFULL

ACCESSION NUMBER:	97:20243 USPATFULL
TITLE:	Hybrid immunoglobulin-thrombolytic enzyme molecules which specifically bind a thrombus, and methods of their production and use
INVENTOR(S):	Quertermous, Thomas, Nashville, TN, United States Runge, Marschall S., Atlanta, GA, United States Haber, Edgar, Salisbury, NH, United States
PATENT ASSIGNEE(S):	The General Hospital Corporation, Boston, MA, United States (U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5609869	19970311
APPLICATION INFO.:	US 1995-453779	19950530 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1993-96173, filed on 26 Jul 1993 which is a continuation-in-part of Ser. No. US 1993-2861, filed on 15 Jan 1993 And Ser. No. US 1990-589435, filed on 27 Sep 1990 which is a continuation-in-part of Ser. No. US 1989-435485, filed on 7 Jul 1989, now abandoned , said Ser. No. US -2861 which is a continuation of Ser. No. US 1988-234051, filed on 19 Aug 1988, now abandoned

DOCUMENT TYPE:	Utility
PRIMARY EXAMINER:	Nucker, Christine M.
ASSISTANT EXAMINER:	Scheiner, Laurie
LEGAL REPRESENTATIVE:	Sterne, Kessler, Goldstein & Fox, P.L.L.C.
NUMBER OF CLAIMS:	5
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	37 Drawing Figure(s); 33 Drawing Page(s)
LINE COUNT:	3876

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Hybrid immunoglobulin-enzyme molecules are provided which are composed of antibodies, or derivatives or fragments thereof, which specifically bind an arterial or venous thrombus that are operably linked to the enzymatically active portions of thrombolytic enzymes such as plasminogen activators. In a preferred embodiment the hybrid molecules specifically bind to fibrin and have fibrinolytic activity. The hybrid molecules of the present invention may be produced by any means, including chemical conjugation, or by means of recombinant DNA, genetic engineering and/or hybridoma technology. Methods for making and using the molecules in diagnosis and therapy are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 424/133.100
INCLS: 424/134.100; 424/136.100; 424/139.100; 424/178.100; 424/192.100; 435/069.300; 435/252.300; 435/172.200; 435/172.300; 530/387.300; 530/388.250; 530/389.300; 536/023.400; 536/023.530
NCL NCLM: 424/133.100
NCLS: 424/134.100; 424/136.100; 424/139.100; 424/178.100; 424/192.100; 435/069.300; 435/252.300; 530/387.300; 530/388.250; 530/389.300; 536/023.400; 536/023.530

L36 ANSWER 20 OF 20 USPATFULL
ACCESSION NUMBER: 96:101563 USPATFULL
TITLE: Method of inducing gene expression by ionizing radiation
INVENTOR(S): Ohno, Tsuneya, Boston, MA, United States
Weichselbaum, Ralph R., Chicago, IL, United States
Kufe, Donald W., Wellesley, MA, United States
PATENT ASSIGNEE(S): Arch Development Corporation, Chicago, IL, United States (U.S. corporation)

	NUMBER	DATE	
PATENT INFORMATION:	US 5571797	19961105	
APPLICATION INFO.:	US 1994-241863	19940511	(8)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Campell, Bruce R.
LEGAL REPRESENTATIVE: Arnold White & Durkee
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 3580
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a method for delivering ionizing radiation to specific tissues, resulting in the activation of a DNA molecule comprising a radiation responsive enhancer-promoter operatively linked to an encoding region that encodes at least one polypeptide. The radiation source may be will generally be in the form of a radionuclide, capable of gamma or beta emissions. Processes for regulating polypeptide expression and inhibiting tumor growth using such DNA molecules are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
INCL INCLM: 514/044.000
INCLS: 424/001.110; 424/001.490; 424/001.610; 424/001.650; 424/001.690; 424/450.000; 424/093.200; 424/093.210; 435/172.300; 435/320.100; 435/069.100; 435/069.500;